

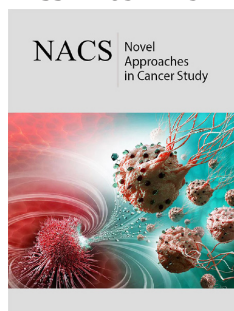
# Mathematical Modeling and Analysis of Leukaemia Transmission: Homotopy Perturbation Method

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## Abstract

Leukaemia is a cancer of the early blood-forming cells. Most often, Leukaemia is a cancer of the white blood cells, but some Leukaemia starts in other blood cell types. This paper discusses two mathematical models: Leukaemia without control and Leukaemia with control. Both models involved a system of nonlinear differential equations. We solve both models by employing the homotopy perturbation method. We propose showing the effectiveness of immune-boosting drugs and immunotherapy to defend Leukaemia cancer cells in the blood.

**Keywords:** Blood cancer; Leukaemia; Immuno therapy; Nonlinear differential equations; Homotopy perturbation method

## Introduction

Leukaemia is a broad term for cancers of the blood cells. The type of Leukaemia depends on the type of blood cell that becomes cancer and whether it grows quickly or slowly. There are several types of Leukaemia, which are divided based mainly on whether the Leukaemia is acute (fast-growing) or chronic (slower growing) and whether it starts in myeloid cells or lymphoid cells [1]. Leukaemia occurs most often in adults older than 55, but it is also the most common cancer in children younger than 15. Explore the links on this page to learn more about the types of Leukaemia plus treatment, statistics, research, and clinical trials. NCI does not have any evidence-based information about the prevention of Leukaemia [2,3].

Leukaemia is grouped in two ways: the type of white blood cell affected - lymphoid or myeloid; and how quickly the disease develops and worsens. Acute leukaemia appears suddenly and multiplies, while chronic leukaemia appears gradually and develops slowly over months to years. This information refers to four types of leukaemia; acute lymphoblastic leukaemia, chronic lymphocytic leukaemia, acute myeloid leukaemia and chronic myeloid leukaemia. The cause of acute leukaemia is unknown, but factors that put some people at higher risk are:

- A. Exposure to intense radiation.
- B. Exposure to certain chemicals, such as benzene.
- C. Certain viral infections (Viruses like the Human T-cell/ leukaemia virus)
- D. Certain genetic syndromes.

The Philadelphia chromosome is defective in most persons diagnosed with chronic myeloid Leukaemia. It has also been related to high levels of radiation exposure [4]. In addition, certain irregularities in the blood cause the cell to grow hastily, and these abnormal cells rule healthy blood cells in the bone marrow. Consequently, the three types of blood cells (white blood cells/T cells, red blood cells, and platelets) gradually die out from the blood. Leukemia disease doesn't cure entirely because of its setbacks in the blood. Despite this, it is indispensable to control this distressing disease, Leukaemia and Khatun et al. [5] purpose, optimal control theory to discuss the optimization of Leukaemia.

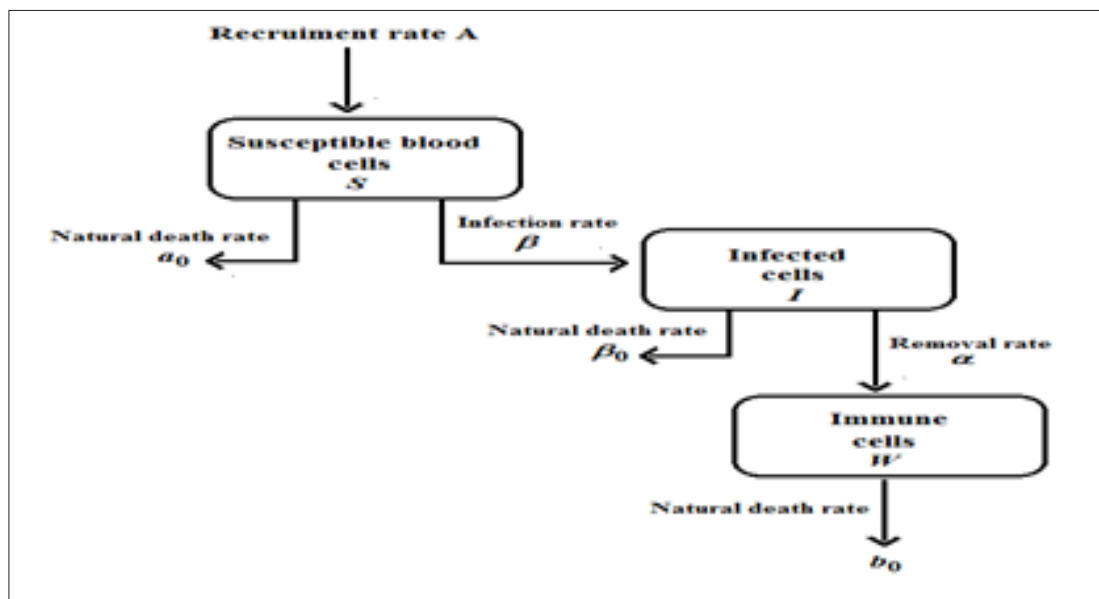
Optimal control theory is an influential mathematical tool used to make decisions involving critical biological situations. It is often used to control the spread of most diseases [6-7]. Many of the researchers investigated about Optimal control theory for various diseases. For example, Moore and Li used a simple mathematical model to study the dynamics of chronic myelogenous leukaemia [8]. Nowak et al. [9] suggested a rigorous mathematical study of cancer immunotherapy. Blaineh et al. [10] presented an optimal control investigation of the dynamics of a vector-transmitted disease using two deterministic models. Eryn et al. [11] and the national cancer institute [12] developed a simple mathematical model of Leukaemia to study the dynamics of it and then apply optimal control theory to analyse the optimal strategy of the treatment of Leukaemia using immune-boosting drugs and adoptive T cell therapy.

In this paper, the mathematical model of Leukaemia is discussed. The model has non-linear equations which represent rates of change for susceptible cells, infected cells as well as immune cells. We used the Homotopy Perturbation Method to solve the system of non-linear equations. Recently a modified approach of the Homotopy Perturbation Method has been used to derive an

approximate analytical expression for each of the nine different groups that form population in HIV/AIDS transmission dynamics [13].

### Mathematical Model of Leukaemia without Control

In this paper, we discuss the model which depicts leukaemia transmission in three compartments. (Figure 1) represents the Flowchart of the model of leukaemia transmission without control. The three compartments are susceptible cells *S*, infected cells *I* and immune cells *W*. In these compartments which are not infected with leukaemia disease but can be infected is defined as susceptible compartment denoted by *S*. The compartment which is infected with leukaemia and able to transmit leukaemia is defined as infective compartment and denoted by *I*. Again, recovered individuals are those who are removed from the susceptible-infective interaction by recovery with immunity, isolation or any process is defined as recovered compartment and denoted by *W*. Further, let *A* be the rate at which the susceptible blood cells entering into the circulatory blood from compartments like bone marrow, lymph nodes and thymus.



**Figure 1:** Schematic diagram of the model of leukemia transmission (without optimal control).

The natural mortality rates of vulnerable blood cells, infected cells, and immune cells are represented by the parameters  $a_0$ ,  $\alpha_0$  and  $b_0$ , respectively. The infection rate of vulnerable blood cells is the metric. The rate at which infected cells recover after contact with immune cells is represented by  $\alpha$ . As a result, this resurrected phrase has been added to the immune cells compartment. The equations that govern our model are as follows:

$$\frac{ds(t)}{dt} = A - \alpha_0 S(t) - \beta S(t)I(t) \quad (1)$$

$$\frac{dI(t)}{dt} = \beta S(t)I(t) - (\beta_0 + \alpha)I(t) \quad (2)$$

$$\frac{dW(t)}{dt} = \alpha I(t) - b_0 W(t) \quad (3)$$

with the initial conditions are

$$S(0) = S_0, I(0) = I_0, W(0) = W_0 \quad (4)$$

### Mathematical Model of Leukaemia with Control

The model with control, which illustrates leukaemia transmission in three compartments, is discussed in this section. We insert two control variables, represented by  $u$ , into the dynamics ( $u_1, u_2$ ). Leukaemia is caused by two mutations in the cell's DNA (chromosome translocation and Philadelphia Chromosome). Some risk factors for leukaemia include cigarette smoking, alcohol, drug usage, and blood problems (such as Li-Fraumeni syndrome, Down syndrome, Bloom syndrome, and other medical illnesses). As far as we know, there are no viable vaccines or medications available to cure leukaemia in the blood entirely.

After being infected with leukaemia, the disease can be controlled with I immune-boosting medications or chemotherapy, (ii) adoptive T cell treatment (also known as gene therapy) or immunotherapy, which harness the patient's immune system's ability to fight disease. As a result, our control  $u_1(t)$  is concerned

with treating immune-boosting medications, whereas  $u_2(t)$  is concerned with the immunotherapeutic treatment of leukaemia cure. We depict the flowchart presentation of the compartmental model with the regulation of leukaemia transmission in (Figure 2) using these assumptions. We can reformulate the model (1) of the following using the previous figure.

$$\frac{ds(t)}{dt} = A - \alpha_0 S(t) - \beta S(t)I(t) = u_1 S(t) \quad (5)$$

$$\frac{dI(t)}{dt} = \beta S(t)I(t) - (\beta_0 + \alpha)I(t) = u_2 S(t) \quad (6)$$

$$\frac{dW(t)}{dt} = \alpha I(t) - b_0 W(t) + u_1 S(t) + u_2 I(t) \quad (7)$$

with the initial conditions are

$$S(0) = S_0, I(0) = I_0, W(0) = W_0 \quad (8)$$

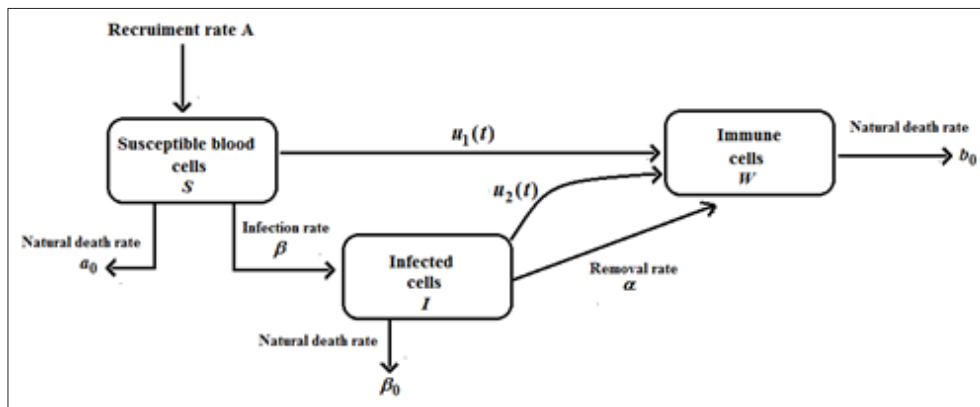


Figure 2: Schematic diagram of the model of leukemia transmission (with control).

### An Analytical Expression for the Susceptible Blood Cells, Infected Cells, Immune Cells in the Treatment of Leukaemia using a Homotopy Perturbation Method

It has been found that several analytical or semi analytical methods for solving nonlinear differential equations even with strong nonlinearities have been developed in recent years. Of these methods, we mention Homotopy analysis method [14,15], Adomian decomposition method [16], variational iteration method [17], Green's function iterative method [18,19], Homotopy Perturbation Method (HPM) [20-22] and Agbariganji Method [23-26] the has received great deal of attention [27-30].

By solving Eqs. (1)-(4) using the Homotopy Perturbation Method (Appendix A) we obtain the solution as follows:

$$s(t) = (s_0 - \frac{A}{a_0})e^{-a_0 t} + \frac{A}{a_0} + (\frac{A\beta I_0}{\alpha_0(\beta_0 + \alpha)} - \frac{\beta S_0 I_0}{\beta_0 + \alpha} - \frac{A\beta I_0}{\alpha_0(\alpha_0 - \beta_0 - \alpha)})e^{-\beta_0 t} + \frac{\beta S_0 I_0 e^{-(\beta_0 + \alpha_0)t}}{\beta_0 + \alpha} - \frac{A\beta I_0 e^{-(\beta_0 + \alpha_0)t}}{\alpha_0(\beta_0 + \alpha)} - \frac{A\beta I_0 e^{-(\beta_0 + \alpha)t}}{\alpha_0(\alpha_0 - \beta_0 - \alpha)} \quad (9)$$

$$I(t) = i_0 e^{-(\beta_0 + \alpha)t} + (\frac{\beta S_0 I_0}{\alpha_0} - \frac{A\beta I_0}{\alpha_0^2})e^{-(\beta_0 + \alpha)t} - \frac{\beta S_0 I_0}{\alpha_0} e^{-(\beta_0 + \alpha_0)t} + \frac{i_0 A\beta e^{-(\beta_0 + \alpha_0)t}}{\alpha_0^2} + \frac{i_0 A\beta e^{-(\beta_0 + \alpha)t}}{\alpha_0} \quad (10)$$

$$w(t) = w_0 e^{-b_0 t} - (\frac{\alpha i_0 e^{-b_0 t}}{b_0 - \beta_0 - \alpha} + \frac{\alpha i_0 e^{-(\beta_0 + \alpha)t}}{b_0 - \beta_0 - \alpha}) \quad (11)$$

By solving Eqs. (5)-(8) using the Homotopy Perturbation Method (Appendix B) we obtain the solution as follows:

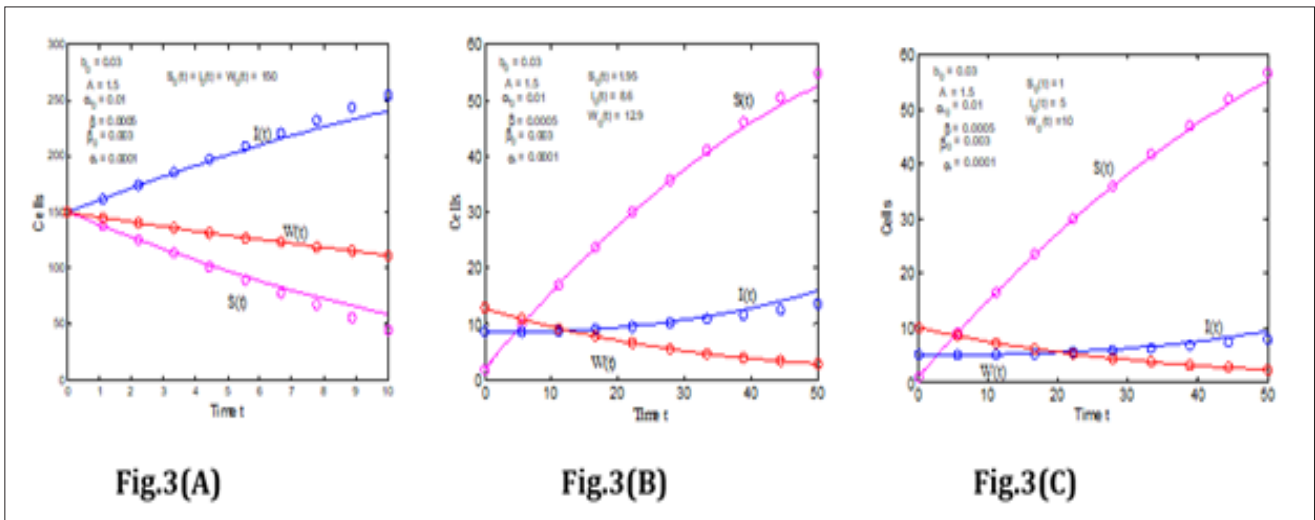
$$s(t) = (s_0 - \frac{A}{a_0 + u_1})e^{-(a_0 + u_1)t} + \frac{A}{a_0 + u_1} + (\frac{\beta I_0}{\beta_0 + \alpha + u_2} - \frac{\beta S_0 I_0}{\beta_0 + \alpha + u_2} - \frac{A}{a_0 + u_1} - \frac{\beta I_0 A e^{-(a_0 + u_1)t}}{(a_0 + u_1)(\beta_0 + \alpha + u_2 - a_0 - u_1)} + \frac{\beta I_0 A e^{-(a_0 + u_1)t}}{(a_0 + u_1)(\beta_0 + \alpha + u_2 - a_0 - u_1)})e^{-(\beta_0 + \alpha + u_2)t} + \frac{\beta I_0 A e^{-(a_0 + u_1)t}}{(a_0 + u_1)(\beta_0 + \alpha + u_2 - a_0 - u_1)} \quad (12)$$

$$I(t) = i_0 e^{-(\beta_0 + \alpha + u_2)t} + \frac{\beta I_0}{a_0 + u_1} (s_0 - \frac{A}{a_0 + u_1}) (e^{-(\beta_0 + \alpha + u_2)t} - e^{-(\beta_0 + \alpha + u_2 + a_0 + u_1)t}) + \frac{I_0 A \beta e^{-(\beta_0 + \alpha + u_2)t}}{(a_0 + u_1)} \quad (13)$$

$$w(t) = w_0 e^{-b_0 t} - (\frac{\alpha + u_2}{b_0 - \beta_0 - \alpha - u_2} - \frac{u_1}{b_0 - a_0 - u_1} (s_0 - \frac{A}{a_0 + u_1}) + \frac{A u_1}{b_0 (a_0 + u_1)}) e^{-b_0 t} + (\frac{\alpha + u_2}{b_0 - \beta_0 - \alpha - u_2} - \frac{u_1}{b_0 - a_0 - u_1} (s_0 - \frac{A}{a_0 + u_1}) - \frac{A u_1}{b_0 (a_0 + u_1)}) e^{-(\beta_0 + \alpha + u_2)t} + \frac{A u_1}{b_0 (a_0 + u_1)} e^{-(\beta_0 + \alpha + u_2)t} \quad (14)$$

### Numerical Simulation

We execute numerical simulations of leukaemia transmission model (1)-(4) and optimal control model (5)-(8) and for which we use a set of logical parameter values. The simulation is performed using ODE45 solver written in MATLAB programming. Eqns. (9)-(12) and Eqns. (13)-(15) are very closed expressions for the models Eqns. (1)-(4) and Eqns.(5)-(8). We compared our analytical solutions obtained by HPM with the numerical simulation obtained by MATLAB software. To test the accuracy of our approximate analytical expressions, the system (1)-(4) and (5)-(8) are also solved by numerically by using MATLAB for all possible values of parameters. The MATLAB program is also given in Appendix C (Figure 3).

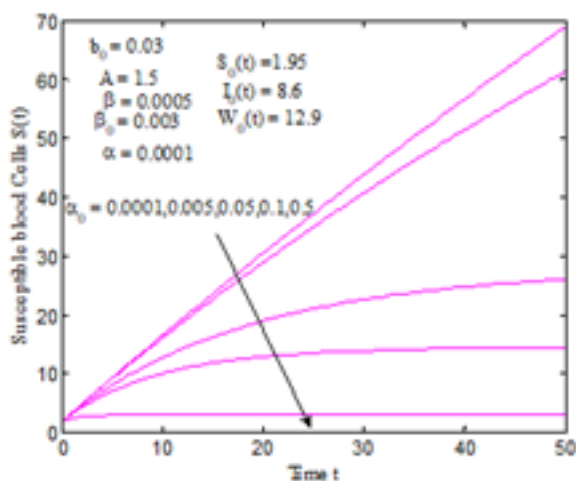


**Figure 3:** Comparison of our analytical expression of SIW with the numerical result for the various values of the parameters using leukemia without control.

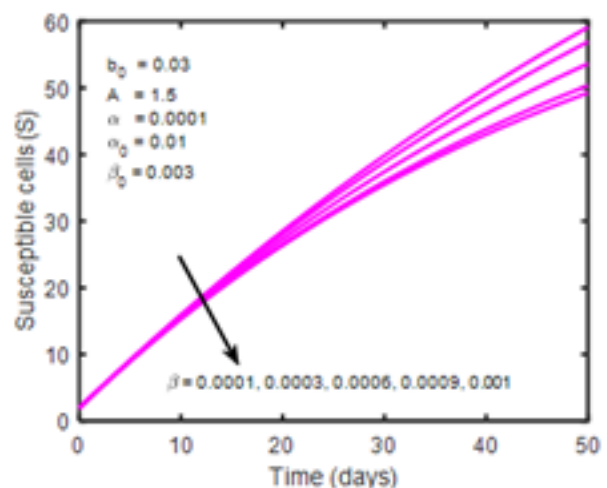
**Discussion**

In treating the Leukaemia model without control, equations (9) to (11) represent the analytical expression for the susceptible blood cells, infected cells, and Immune cells. Equations (12) to (14) provide the analytical expression for the susceptible blood cells, Infected cells, and Immune cells in the Leukaemia model with control.

(Figure 4) and (Figure 5) represents the change in susceptible blood cells and infected cells over 50 days for various infection rates or interaction rates with cancer cells in the patient’s body. For decreasing levels of  $\beta$ , one can see that the number of susceptible blood cells increases. It indicates that as the infection rate rises, the number of susceptible blood cells decreases. This is due to the fact that susceptible blood cells are drawn to infected cells in order to interact with cancer cells in the body.

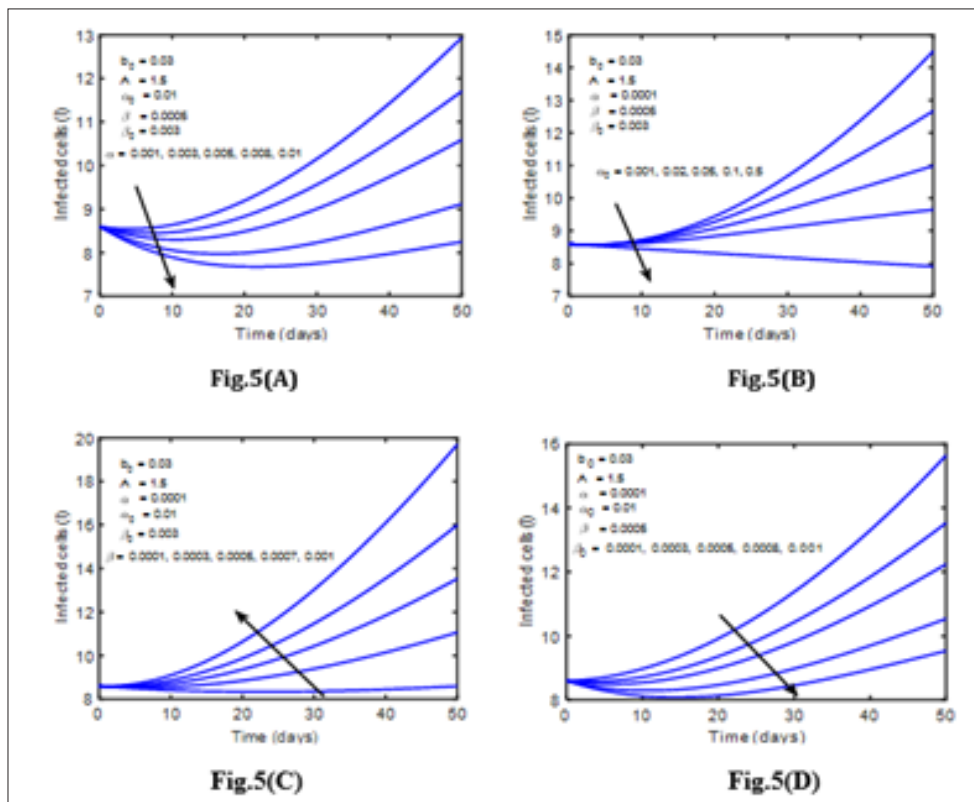


**Fig.4(A)**



**Fig.4(B)**

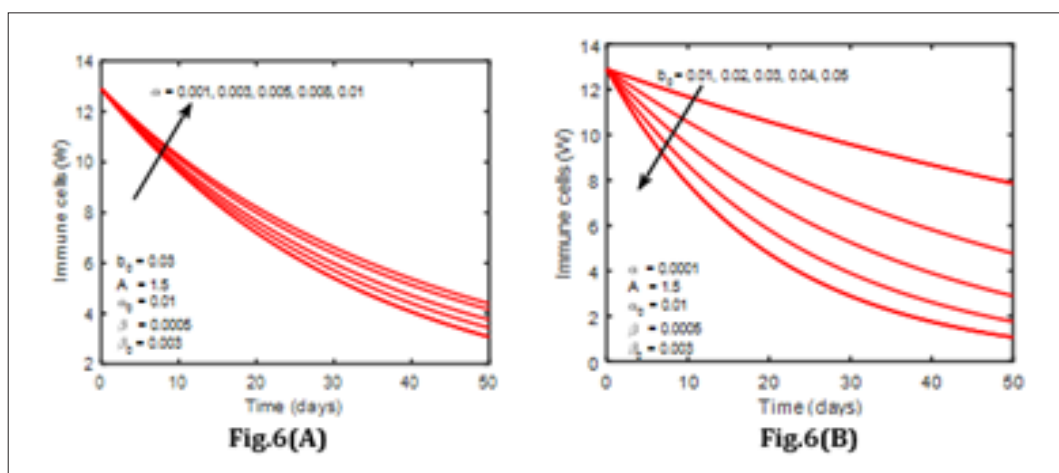
**Figure 4:** The rate of Susceptible cells for various values of  $\alpha_0$  and  $\beta$  (Leukemia without control).



**Figure 5:** The rate of infected cells for various values of  $\alpha$ ,  $\alpha_0$ ,  $\beta$  and  $\beta_0$  (Leukemia without control).

Different phenomena can be observed in infected cells. As the number of infected cells in the blood increases, so does the number of cancer cells infect. It means that when cancer cells interact with susceptible cells, infected cells are produced, and the concentration of infected cells rises substantially as the interaction rate in the blood circulatory system rises. In addition, (Figure 6) depicts the variation of immune cells for various values of  $\beta$ . The

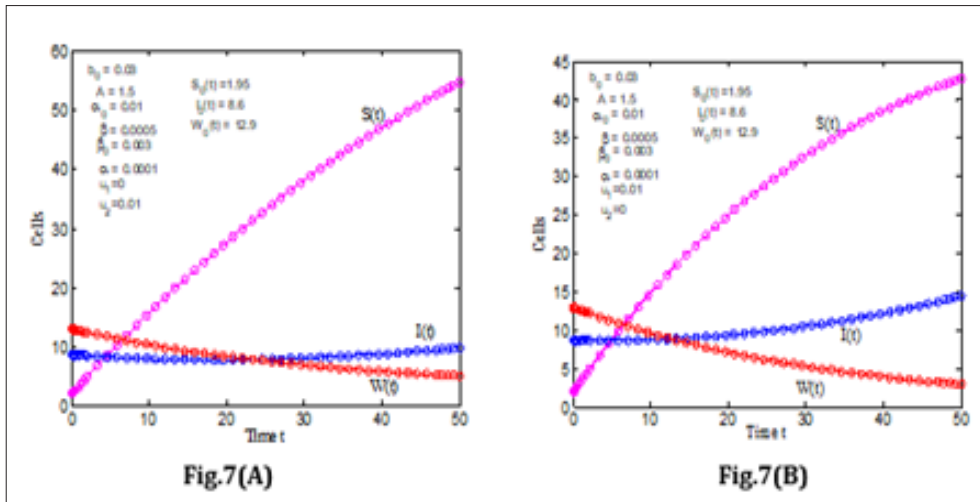
number of immune cells grows as the infection rate in the patient's blood decreases, as seen in (Figure 6). This means that cancer cells interact with immune cells at a lower rate. In normal, human immune cells, also known as T cells, attack infection in the body; but, when infection rates rise, the immune system weakens, and immune cells cannot operate normally.



**Figure 6:** The rate of immune cells for various values of  $\alpha$  and  $b_0$  leukemia without control.

(Figure 7) indicates the variation of susceptible, infected, and immune cells during 50 days with fixed values for other parameters. Moreover, in Figure 7(A), when  $u_1=0, u_2=0.01$ , and in Figure 7(B), when  $u_1=0.01, u_2=0$ , we compared all three cells and the function

of susceptible blood cells and infected cells is rising, whilst the function of immune cells is decreasing. It can be seen in the diagram that the susceptible blood cells are soaring towards higher recovery rates (Table 1).



**Figure 7:** Rate of SIW for the various values of the parameter  $u_1$  and  $u_2$  leukemia with control.

**Table 1:** Susceptible blood cells, Infected cells, Immune cells. (Nomenclature and Units).

Symbol	Name
S	Susceptible blood cells
I	Infected cells
W	Immune cells
t	Time (days)
A	Source term of susceptible population
$\alpha$	Rate at which the infectious individuals recover for immunity
$\alpha_0$	Natural death rate of susceptible cells
$\beta$	Infection rate of susceptible cells due to cancer cells
$\beta_0$	Natural death rate of infected cells
$b_0$	Natural death rate of immune cells
$u_1$	Chemotherapeutic control
$u_2$	Immunotherapeutic treatment control

### Conclusion

We discuss the SIR (Susceptible - Infected - Recovered) model of Leukaemia with two cases in this work. Both models are solved using the Homotopy Perturbation Method, and numerical simulations demonstrate the analytic results. We see that the rate of infected cells and immune cells significantly impacts the disease's spread.

Immunotherapy is now considered to be the most promising cancer treatment. When the number of infected cells rises, the number of immune cells in the body falls. On the other hand, immunotherapy and immune-boosting medicines increase the number of immune cells in a patient. Our study revealed that a combination of the two would be the most effective method to control this disease.

**Appendix A: Analytical solution on nonlinear Eqns. (1)-(4) using Homotopy Perturbation Method (HPM).**

$$\frac{dS}{dt} = A - \alpha_0 S - \beta SI \quad (A.1)$$

$$\frac{dI}{dt} = \beta SI - (\beta_0 + \alpha)I \quad (A.2)$$

$$\frac{dW}{dt} = \alpha I - b_0 W \quad (A.3)$$

with the initial conditions are

$$S(0) = S_0, I(0) = I_0, W(0) = W_0 \quad (A.4)$$

The Homotopy form the Eqns. (A.1) -(A.4) can be constructed as follows:

$$(1-p)\left(\frac{ds}{dt} - A + \alpha_0 S\right) + p\left(\frac{ds}{dt} - A + \alpha_0 S + \beta SI\right) = 0 \quad (A.5)$$

$$(1-p)\left(\frac{dI}{dt} + (\beta_0 + \alpha)I\right) + p\left(\frac{dI}{dt} - \beta SI + (\beta_0 + \alpha)I\right) = 0 \quad (A.6)$$

$$(1-p)\left(\frac{dW}{dt} + b_0 W\right) + p\left(\frac{dW}{dt} - \alpha I + b_0 W\right) = 0 \quad (A.7)$$

where  $P$  is the embedding parameter and  $p \in [0, 1]$ , The approximate solution of (A.5) to (A.7) are

$$S = S_0 + pS_1 + p^2S_2 + \dots, I = I_0 + pI_1 + p^2I_2 + \dots, W = W_0 + pW_1 + p^2W_2 + \dots \quad (A.8)$$

Substituting Eqns. (A.8) into (A.5) -(A.7), gives the following result.

$$(1-p)\left(\frac{d}{dt}(S_0 + pS_1 + \dots) - A + \alpha_0(S_0 + pS_1 + \dots)\right) + p\left(\frac{d}{dt}(S_0 + pS_1 + \dots) - A + \alpha_0(S_0 + pS_1 + \dots) + \beta(S_0 + pS_1 + \dots)(I_0 + pI_1 + \dots)\right) = 0 \quad (A.9)$$

$$(1-p)\left(\frac{d}{dt}(I_0 + pI_1 + \dots) + (\beta_0 + \alpha)(I_0 + pI_1 + \dots)\right) + p\left(\frac{d}{dt}(I_0 + pI_1 + \dots) - \beta(S_0 + pS_1 + \dots)(I_0 + pI_1 + \dots) + (\beta_0 + \alpha)(I_0 + pI_1 + \dots)\right) = 0 \quad (A.10)$$

$$(1-p)\left(\frac{d}{dt}(W_0 + pW_1 + \dots) + b_0(W_0 + pW_1 + \dots)\right) + p\left(\frac{d}{dt}(W_0 + pW_1 + \dots) - \alpha(I_0 + pI_1 + \dots) + b_0(W_0 + pW_1 + \dots)\right) = 0 \quad (A.11)$$

Comparing the coefficients of like powers of p in Eqn. (A.8) gives:

$$p^0 : \frac{dS_0}{dt} - A + \alpha_0 S_0 = 0 \quad (A.11)$$

$$p^1 : \frac{dS_1}{dt} - A + \alpha_0 S_1 + \beta S_0 I_0 = 0 \quad (A.12)$$

The initial conditions are,

$$S_0(t=0) = s_0, S_1(t=0) = 0, S_2(t=0) = 0 \quad (A.13)$$

The solution of the Eqns. (A.11) and (A.12) are given by

$$S_0 = \left(s_0 - \frac{A}{\alpha_0}\right)e^{-\alpha_0 t} + \frac{A}{\alpha_0} \quad (A.14)$$

$$S_1 = \left(\frac{A\beta I_0}{\alpha_0(\beta_0 + \alpha)} - \frac{\beta S_0 I_0}{\alpha_0(\alpha_0 - \beta_0 - \alpha)}\right)e^{-\alpha_0 t} + \frac{\beta S_0 I_0 e^{-(\beta_0 + \alpha_0 + \alpha)t}}{\beta_0 + \alpha} - \frac{A\beta I_0 e^{-(\beta_0 + \alpha_0 + \alpha)t}}{\alpha_0(\beta_0 + \alpha)} - \frac{A\beta I_0 e^{-(\beta_0 + \alpha)t}}{\alpha_0(\alpha_0 - \beta_0 - \alpha)} \quad (A.15)$$

Comparing the coefficients of like powers of p in Eqn. (A.9) gives:

$$p^0 = \frac{dI_0}{dt} + (\beta_0 + \alpha)I_0 = 0 \quad (A.16)$$

$$p^1 = \frac{dI_1}{dt} + (\beta_0 + \alpha)I_1 - \beta S_0 I_0 = 0 \quad (A.17)$$

The initial conditions are,

$$I_0(t=0) = i_0, I_1(t=0) = 0, I_2(t=0) = 0 \quad (A.18)$$

The solution of the Eqns. (A.16) and (A.17) are given by

$$I_0(t) = i_0 e^{-(\beta_0 + \alpha)t} \quad (A.19)$$

$$I_1(t) = \left(\frac{\beta S_0 I_0}{\alpha_0} - \frac{A\beta I_0}{\alpha_0^2}\right)e^{-(\beta_0 + \alpha)t} - \frac{\beta S_0 I_0}{\alpha_0} e^{-(\beta_0 + \alpha_0 + \alpha)t} + \frac{i_0 A \beta e^{-(\beta_0 + \alpha_0 + \alpha)t}}{\alpha_0^2} + \frac{i_0 A \beta e^{-(\beta_0 + \alpha)t}}{\alpha_0} \quad (A.20)$$

Comparing the coefficients of like powers of p in Eqn. (A.10) gives:

$$p^0 : \frac{dW_0}{dt} + b_0 W_0 = 0 \quad (A.21)$$

$$p^1 : \frac{dW_1}{dt} + b_0 W_1 - \alpha I_0 = 0 \quad (A.22)$$

The initial conditions are,

$$W_0(t=0) = w_0, W_1(t=0) = 0, W_2(t=0) = 0 \quad (A.23)$$

The solution of the Eqns. (A.21) and (A.22) are given by

$$W_0(t) = w_0 e^{-b_0 t} \quad (A.24)$$

$$W_1(t) = -\frac{\alpha I_0 e^{-b_0 t}}{b_0 - \beta_0 - \alpha} + \frac{\alpha I_0 e^{-(\beta_0 + \alpha)t}}{b_0 - \beta_0 - \alpha} \quad (A.25)$$

**Appendix B: Analytical solution on nonlinear Eqns. (5)-(8) using Homotopy Perturbation Method (HPM).**

Consider the differential equation

$$\frac{dS}{dt} = A - \alpha_0 S - \beta SI - u_1 S \quad (B.1)$$

$$\frac{dI}{dt} = \beta SI - (\beta_0 + \alpha)I - u_2 I \quad (B.2)$$

$$\frac{dW}{dt} = \alpha I - b_0 W + u_1 S + u_2 I \quad (B.3)$$

with the initial conditions are

$$S(0) = S_0, I(0) = I_0, W(0) = W_0 \quad (B.4)$$

The Homotopy form the Eqns. (B.1) -(B.3) can be constructed as follows:

$$(1-p)\left(\frac{dS}{dt} - A + (\alpha_0 + u_1)S\right) + p\left(\frac{dS}{dt} - A + (\alpha_0 + u_1)S + \beta SI\right) = 0 \quad (B.5)$$

$$(1-p)\left(\frac{dI}{dt} + (\beta_0 + \alpha + u_2)I\right) + p\left(\frac{dI}{dt} - \beta SI + (\beta_0 + \alpha + u_2)I\right) = 0 \quad (B.6)$$

$$(1-p)\left(\frac{dW}{dt} + b_0 W\right) + p\left(\frac{dW}{dt} - \alpha I - b_0 W + u_1 S + u_2 I\right) = 0 \quad (B.7)$$

where is the embedding parameter and  $p \in [0,1]$ , The approximate solution of (B.5) to (B.7) are

$$S = S_0 + pS_1 + p^2S_2 + \dots, I = I_0 + pI_1 + p^2I_2 + \dots, W = W_0 + pW_1 + p^2W_2 + \dots \quad (B.8)$$

Substituting Eqns. (B.8) into (B.5) - (B.7), gives the following result.

$$(1-p)\left(\frac{d}{dt}S_0 + pS_1 + \dots\right) - A + (\alpha_0 + u_1)(S_0 + pS_1 + \dots) + p\left(\frac{d}{dt}S_1 + pS_2 + \dots\right) - A + (\alpha_0 + u_1)(S_0 + pS_1 + \dots) + \beta(S_0 + pS_1 + \dots)(I_0 + pI_1 + \dots) = 0 \quad (B.9)$$

$$(1-p)\left(\frac{d}{dt}I_0 + (\beta_0 + \alpha + u_2)(I_0 + pI_1 + \dots)\right) + p\left(\frac{d}{dt}I_1 + pI_2 + \dots\right) - \beta(S_0 + pS_1 + \dots)(I_0 + pI_1 + \dots) + (\beta_0 + \alpha + u_2)(I_0 + pI_1 + \dots) = 0 \quad (B.10)$$

$$(1-p)\left(\frac{d}{dt}W_0 + pW_1 + \dots\right) + b_0(W_0 + pW_1 + \dots) + p\left(\frac{d}{dt}W_1 + pW_2 + \dots\right) - \alpha I + b_0(W_0 + pW_1 + \dots) - u_1(S_0 + pS_1 + \dots) - u_2(I_0 + pI_1 + \dots) = 0 \quad (B.11)$$

Comparing the coefficients of like powers of p in Eqn. (B.9) gives:

$$p^0 : \frac{dS_0}{dt} - A + (\alpha_0 + u_1)S_0 = 0 \quad (B.12)$$

$$p^1 : \frac{dS_1}{dt} - A + (\alpha_0 + u_1)S_1 + \beta S_0 I_0 = 0 \quad (B.13)$$

The initial conditions are,

$$S_0(t = 0) = s_0, S_1(t = 0) = 0, S_2(t = 0) = 0 \quad (B.14)$$

The solution of the Eqns. (B.12) & (B.13) are given by

$$S_0 = \left(s_0 - \frac{A}{\alpha_0 + u_1}\right)e^{-(\alpha_0 + u_1)t} + \frac{A}{\alpha_0 + u_1} \quad (B.15)$$

$$S_1(t) = -\frac{\beta I_0 A e^{-(\alpha_0 + u_1)t}}{(\alpha_0 + u_1)(\beta_0 + \alpha + u_2 - \alpha_0 - u_1)} + \frac{\beta I_0}{\beta_0 + \alpha + u_2} \left(s_0 - \frac{A}{\alpha_0 + u_1}\right) e^{-(\beta_0 + \alpha + u_2 + \alpha_0 + u_1)t} + \frac{\beta I_0 A e^{-(\beta_0 + \alpha + u_2)t}}{(\alpha_0 + u_1)(\beta_0 + \alpha + u_2 - \alpha_0 - u_1)} \quad (B.16)$$

Comparing the coefficients of like powers of p in Eqn. (B.10) gives:

$$p^0 : \frac{dI_0}{dt} + (\beta_0 + \alpha + u_2)I_0 = 0 \quad (B.17)$$

$$p^1 : \frac{dI_1}{dt} + (\beta_0 + \alpha + u_2)I_1 - \beta S_0 I_0 = 0 \quad (B.18)$$

The initial conditions are,

$$I_0(t = 0) = i_0, I_1(t = 0) = 0, I_2(t = 0) = 0 \quad (B.19)$$

The solution of the Eqns. (B.17) and (B.18) are given by

$$I_0(t) = i_0 e^{-(\beta_0 + \alpha + u_2)t} \quad (B.20)$$

$$I_1(t) = \frac{\beta I_0}{\alpha_0 + u_2} \left(s_0 - \frac{A}{\alpha_0 + u_1}\right) (e^{-(\beta_0 + \alpha + u_2)t} - e^{-(\beta_0 + \alpha + u_2 + \alpha_0 + u_1)t}) + \frac{t i_0 A \beta e^{-(\beta_0 + \alpha + u_2)t}}{(\alpha_0 + u_1)} \quad (B.21)$$

Comparing the coefficients of like powers of p in Eqn. (B.11) gives:

$$p^0 : \frac{dW_0}{dt} + b_0 W_0 = 0 \quad (B.22)$$

$$p^1 : \frac{dW_1}{dt} + b_0 W_1 - \alpha I_0 - u_1 S_0 - u_2 I_0 = 0 \quad (B.23)$$

The initial conditions are,

$$W_0(t = 0) = w_0, W_1(t = 0) = 0, W_2(t = 0) = 0 \quad (B.24)$$

The solution of the Eqns. (B.22) & (B.23) are given by

$$W_0(t) = w_0 e^{-b_0 t} \quad (B.25)$$

$$W_1(t) = \left(\frac{(\alpha + u_1)u_1}{b_0 - \beta_0 - \alpha - u_2} + \frac{u_1}{b_0 - \alpha_0 - u_1} \left(s_0 - \frac{A}{\alpha_0 + u_1}\right) + \frac{A u_1}{b_0 (\alpha_0 + u_1)}\right) e^{-b_0 t} + \frac{(\alpha + u_1)u_1}{b_0 - \beta_0 - \alpha - u_2} e^{-(\beta_0 + \alpha + u_2)t} + \frac{u_1}{b_0 - \alpha_0 - u_1} \left(s_0 - \frac{A}{\alpha_0 + u_1}\right) e^{-(\alpha_0 + u_1)t} + \frac{A u_1}{b_0 (\alpha_0 + u_1)} \quad (B.26)$$

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