A MATHEMATICAL MODEL OF HUMAN IMMUNE SYSTEM'S RESPONSE TO CHRONIC MYELOID LEUKEMIA USING THE INTERACTION BETWEEN NAIVE T CELLS, EFFECTOR T CELLS, AND CML CANCER CELLS OVER A PERIOD OF TIME

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Abstract

In this research work, we proposed and analysed a mathematical model for chronic myeloid leukemia (CML), a cancer of the blood. In particular we developed a model for the interaction between naive T cells, effector T cells and the CML cancer cells in the body, using a system of ordinary differential equations. We made reasonable assumptions about the model and conduct a linear stability analysis. We also constructed the phase portrait for the model and obtained the numerical solutions. We obtained values for the Parameters from available experimental data and estimated and analysed the system for sensitivity to changes in the parameters. Our results indicated that the most promising research avenues for treatment of CML should be those that affect the two significant parameters i.e. CML growth and death rates.

Key words: **Chronic Myeloid Leukemia, Mathematical Model, Immune System, Naive T cells, Effector T cells.**

1.0.Introduction

Currently the human population has grown into a reasonable extent, and there are several diseases that affect people and have not been taken into consideration. A couple of this human population has gone into extinction as a result of migration, epidemics, civilization and war (Akinwande, 2009). Leukemia is a progressive, malignant disease characterized by a rapid and uncontrolled proliferation and growth of abnormal blood cells. This proliferation occurs in the bone marrow, as well as in the peripheral blood, blood forming organs, and blood filtering organs. The classification of different forms of leukemia relies on the progression of the disease (acute or chronic) as well as the type of cell affected (myeloid, Lymphoid, or monocyte) (Bruce et al., 1994).

Chronic Myeloid Leukaemia (CML) is a cancer of the bone marrow and blood (Leukemia and Lymphoma Society, 2012). It is a form of leukemia characterised by the increased and unregulated growth of predominantly myeloid cells in the bone marrow and the accumulation of these cells in the blood. It is characterised by the excessive build up of relatively matured but still abnormal, white blood cells, typically taking months or years to progress. The cells are produced at much higher rates, resulting in many abnormal white blood cells. It is

for some time before treatment to ensure maximum effectiveness of the therapy. Chronic myeloid leukaemia occurs in all age groups, but mostly common in the middle-aged and the elderly. Its annual incidence is 1-2 per 100,000 people, and slightly more men than women are affected. CML represents about 15-20% of all the cases of adult leukemia in western populations (Faderl et al., 1999).The only well described risk factor of CML is exposure to ionizing radiation for example, increased rate of CML were seen in people exposed to the atomic bombings of Hiroshima and Nagasaki (Moloney, 1987). Leukemia is also rarely associated with pregnancy, affecting only about 1 in 10,000 pregnant women. (Shapira et al., 2008). Chronic myeloid Leukemia can be treated with relative safety at any time during the pregnancy with interferon-alpha hormones (Shapira et al., 2008).

The standard treatment for CML is the tyrosine kinase inhibitor imatinib mesylate (marketed as Gleevec or Glivec) (Angstreich et al., 2004). Although imatinib is an effective treatment for CML and most patients attain some form of remission, imatinib does not completely eliminate all leukemia cells, and if the imatinib treatment is stopped, most patients eventually relapse (Cortes et al., 2005).The current main treatments for CML are radiation, Chemotherapy, bone marrow transplant and the drug Gleevec (imatinib) (Schiffer et al., 2003). Chronic myeloid leukemia (CML) affects mostly adults although children are diagnosed with CML too. The chance of getting chronic myeloid leukemia increases in people aged 65 years and older. However people can develop chronic myeloid leukemia at any age. An estimate of 26,359 people living with (or in remission from) CML as of January 1, 2008 (Leukemia and Lymphoma Society, 2012).

Chronic myeloid leukemia is caused by an abnormal chromosome in a particular blood cell line. People with CML have an abnormal chromosome called the Philadelphia chromosome (Ph chromosome). The Ph chromosome is the result of a translocation between chromosomes 22 and 9. The translocation leads to the development of a cancer-causing gene (oncogene) called the *Bcr-Abl* gene. The initiating factor that creates the abnormal chromosome is not known, but both genetic and environmental factors may play a role. In particular, radiation exposure or therapy for a prior cancer can damage the Deoxyribonucleic acid (DNA) or cause mutations (Leukemia and Lymphoma Society, 2012).

2.0. Materials and Method

2.1. Model Formulation

Let t, represent time, measured in days .We consider the following population of cells in the circulating blood system, measured as concentrations of cells per µl:

T_n = Naïve T cells

T_e = Effector T cells specific to CML

C=Chronic Myeloid Leukemia (CML) cancer cells

Each of the three cell population is a function of time t.

The naïve T cells population consists of all naïve T cells, both specific and non-specific for CML. The naïve T cells either have not yet been exposed to CML antigen, or else are not CML-specific.

The effector T cells have differentiated from naïve T cells upon activation by a CML antigen and co stimulators.

The system of differential equations is given below,

$$\left.\begin{aligned} \frac{dT_n}{dt} &= s_n - d_n T_n - k_n T_n\left(\frac{C}{C+\eta}\right) \\ \frac{dT_e}{dt} &= \alpha_n k_n T_n\left(\frac{C}{C+\eta}\right) + \alpha_e T_e\left(\frac{C}{C+\eta}\right) - d_e T_e - \gamma_e C T_e \\ \frac{dC}{dt} &= r_c C \ln\left(\frac{C_{max}}{C}\right) - d_c C - \gamma_c C T_e \end{aligned}\right\} \qquad (2.1)$$

s_n = A source term for new T cells entering the blood system.

d_n = The naive T cells death rate constant which is equal to the reciprocal of the average lifespan of a T_n cell, and can be thought of as roughly approximating the fraction of the T_n population that is expected to die naturally in 1 day.

η = The standard half-saturated concentration in a michaelis-menten term.

k_n = The rate constant which makes $k_n T_n\left(\frac{C}{C+\eta}\right)$, equal to the instantaneous rate of T_n loss due to encounter between naive T cells and CML antigen.

α_n = The coefficient that incorporates the rate at which the encounter between T_n and professional APC lead to the activation of T_n as well as the rates of proliferation and differentiation into T_e.

α_e = A recruitment term that is represented as michaelis-menten which incorporates the recruitment of other immune cells to aid in killing CML.

d_e = The death rate for T_e.

γ_e = The death rate constant for loss of T_e due to the encounter between T_e and CML cancer cells.

r_c = Contribution due to the growth of C in the form of a Gompertz law.

C_{max} = Estimate of the maximum possible concentration of CML

d_c = The loss of CML cells which die a natural death i.e. death rate of C

γ_c = The loss of C due to encounter with T_e.

We shall use the following initial values for the three populations where t = 0 is the starting time for the model:

$T_n(0)$= 1510 cells/ μ l, $T_e(0)$ = 20 cells/ μ l, C (0) = 10,000 cells/ μ

To further simplify the model for ease of quantitative analysis, the numbers of parameters are further reduced by making reasonable assumptions about the model.

(a) Activation rate k_n is assumed to be the same as recruitment rate α_e i.e. $\alpha_e = k_n = k$

(b) Death of C by T_e contact γ_e is assumed to be the same as the death of T_e by C contact, γ_c i.e. $\gamma_c = \gamma_e = \gamma$

(c) T_e proliferation α_n is assumed to be the same as one unit i.e. $\alpha_n = 1$

(d) T_e death rate d_e, T_n death rate d_n and C death rate d_c are assumed to be equal to d i.e. $d_e = d_n = d_c = d$

Now, substituting the new coefficients into equation (2.1), we have

$$\left.\begin{aligned} \frac{dT_n}{dt} &= s_n - dT_n - kT_n\left(\frac{C}{C+\eta}\right), \\ \frac{dT_e}{dt} &= k\left(\frac{C}{C+\eta}\right) + (T_n + T_e) - dT_e - \gamma CT \\ \frac{dC}{dt} &= r_c C \ln\left(\frac{C_{max}}{C}\right) - dC - \gamma CT \end{aligned}\right\} \qquad (2.2)$$

Where,

s_n = T_n source term

d =Death rate

k = Activation rate

η = Michaelis-menten term.

γ =The rate of loss

C_{max} = Maximum C

3.0. Stability Analysis of the Equilibrium States.

3.1. Equilibrium States

We have three types of equilibrium states from (2.2)

1. **Disease free- equilibrium:** This is the equilibrium that is attained by an entire healthy population,
$T_n = T_n^*$, $T_e = 0$, $C = 0$

2. **Collapse equilibrium:** This equilibrium describes the vanishing of the cell population. These are the points
$T_n = 0$, $T_e = 0$, $C = C^*$

3. **Endemic equilibrium:** In this state, the cell population contains healthy and infected T cells. The equilibrium generally takes the form
$T_n = T_n^{**}$, $T_e = T_e^{**}$, $C = C^*$

3.2. Stability Analysis

The jacobian of (2.2) is

$$Df(T_n, T_e, C) = \begin{pmatrix} -d - k\left(\frac{C}{C+\eta}\right) & 0 & -kT_n\left(\frac{\eta}{(C+\eta)^2}\right) \\ kT_n\left(\frac{\eta}{(C+\eta)^2}\right) & k\left(\frac{C}{C+\eta}\right) - d - \gamma C & k(T_n + T_e)\left(\frac{\eta}{(C+\eta)^2}\right) - \gamma T_e \\ 0 & -\gamma C & r_c\left(\ln\left(\frac{C_{max}}{C}\right) - 1\right) \end{pmatrix} \quad (3.1)$$

3.3. Linearization

The linearization of (2.2) at **Disease free- equilibrium** is

$$Df(T_n^*, 0, 0) = \begin{pmatrix} -d & 0 & -\alpha \\ \alpha & -d & \alpha \\ 0 & 0 & \beta \end{pmatrix} \quad (3.2)$$

where

$$\alpha = \left(\frac{kT_n^*}{\eta}\right), \qquad \beta = r_c\left(\ln\left(\frac{C_{max}}{C}\right) - 1\right)$$

For the Eigenvalues, $|A - \lambda I| = 0$

Then,

$$\begin{vmatrix} -(\lambda+d) & 0 & -\alpha \\ \alpha & -(\lambda+d) & \alpha \\ 0 & 0 & \beta-\lambda \end{vmatrix}=0$$

i.e.

$$(\lambda+d)(\lambda+d)(\beta-\lambda)-0(\alpha(\beta-\lambda))-\alpha(0-0)=0$$

Hence,

$$\lambda_1=-d, \qquad \lambda_2=-d, \qquad \lambda_3=-\beta$$

Since $\lambda_1=\lambda_2<0$ .The Eigenvalues are equal and negative. $\lambda_3<0$ Which is also negative Hence the critical point $(T_n^*,0,0)$ is an asymptotically stable proper or improper node of the system.

At **Collapse equilibrium**

$$Df(0,0,C^*)=\begin{pmatrix} -\alpha_1 & 0 & 0 \\ 0 & \beta_1 & 0 \\ 0 & -\alpha_2 & -\beta_2 \end{pmatrix} \qquad (3.3),$$

where

$$\alpha_1=\left(d+k\left(\frac{C^*\cdot}{C^*+\eta}\right)\right), \qquad \beta=k\left(\frac{C^*}{C^*+\eta}\right)-d-\gamma C^*, \quad \alpha_2=\gamma C^*,$$

$$\beta_2=r_c\left(\ln\left(\frac{C_{\max}}{C}\right)-1\right)$$

For the Eigenvalues, we have

$$\begin{vmatrix} -(\lambda+\alpha_1) & 0 & 0 \\ 0 & (\beta_1-\lambda) & 0 \\ 0 & -\alpha_2 & \beta_2-\lambda \end{vmatrix}=0$$

i.e,

$$-(\lambda+\alpha_1)((\beta_1-\lambda)(\beta_2-\lambda)-0)-0(0-0)+0(0-0)=0$$

i.e.

$$\lambda_1=-\alpha_1, \qquad \lambda_2=\beta, \quad \lambda_3=\beta_2$$

Since $\lambda_1<0$, λ_2 *and* λ_3 are greater than 0, then the Eigenvalues are real and the critical point $(0,0,C^*)$ is an unstable improper node of the system.

At **Endemic equilibrium,**

$$Df(T_n^{**}, T_e^{**}, C^*) = \begin{pmatrix} -\alpha_3 & 0 & -\beta_3 \\ \beta_3 & \alpha_4 & \beta_4 \\ 0 & -\beta_5 & \alpha_5 \end{pmatrix} \qquad (3.4)$$

where

$$\alpha_3 = \left(d + k\left(\frac{C^*}{C^* + \eta}\right)\right), \quad \beta_3 = kT_n^{**}\left(\frac{\eta}{(C+\eta)^2}\right), \alpha_4 = k\left(\frac{C^*}{C^* + \eta}\right) - d - \gamma C^*$$

$$\beta_4 = k(T_n^{**} + T^{**}_e)\left(\frac{\eta}{(C^* + \eta)^2}\right) - \gamma T_e^{**}, \quad \beta_5 = -\gamma C^*, \quad \alpha_5 = r_c\left(\ln\left(\frac{C_{\max}}{C}\right) - 1\right)$$

For the Eigenvalues, we have

$$\begin{vmatrix} -(\lambda + \alpha_3) & 0 & -\beta_3 \\ \beta_3 & \alpha_4 - \lambda & \beta_4 \\ 0 & -\beta_5 & \alpha_5 - \lambda \end{vmatrix} = 0$$

i.e.

$$-(\lambda + \alpha_3)((\alpha_4 - \lambda)(\alpha_5 - \lambda) + \beta_4\beta_5) - 0(\beta_3(\alpha_5 - \lambda) - 0) - \beta_3(-\beta_3\beta_5) = 0$$

i.e.

$$-(\lambda + \alpha_3)((\alpha_4 - \lambda)(\alpha_5 - \lambda) + \beta_4\beta_5) + \beta_3^2\beta_5 = 0$$

$$(\lambda + \alpha_3)((\alpha_4 - \lambda)(\alpha_5 - \lambda) + q) - q_1 = 0,$$

where

$$q = \beta_4\beta_5 \quad \text{And} \quad q_1 = \beta_3^2\beta_5$$

Then,

$$\lambda_1 = \frac{1}{6}A - \frac{6B}{A+C}, \quad \lambda_2 = \frac{-1}{12}A + \frac{3B}{A+C} + \frac{1}{2}I\sqrt{3}\left(A + \frac{6B}{A}\right),$$

$$\lambda_3 = \frac{-1}{12}A + \frac{3B}{A+C} - \frac{1}{2}I\sqrt{3}\left(\frac{1}{6}A + \frac{6B}{A}\right),$$

where

$$A = (-13\alpha_4\alpha_5 - 13\alpha_4\alpha_5^2 - 48\alpha_3\alpha_4\alpha_5 - 36q\alpha_4 - 36q\alpha_5 - 72\alpha_3 q + 12\alpha_4\alpha_5^2 - 12\alpha_5^3\alpha_4 + 12\alpha_4\alpha_5^3 - 12\alpha_5^3\alpha_5 + 108q_1 + 81\alpha_4^4 + 81\alpha_5^4 - 81\alpha_5^4 + 12(6\alpha_4\alpha_5\alpha_5^4 - 6\alpha_4^4\alpha_5\alpha_5 - 6\alpha_4^4\alpha_5\alpha_5 + 6\alpha_4^2\alpha_5\alpha_5^3 - 6\alpha_4\alpha_5^3\alpha_5 + 6\alpha_4\alpha_5^3\alpha_5^3 + 6\alpha_4\alpha_5^3\alpha_5^3 + 6\alpha_4\alpha_5^2\alpha_5^3 + 18\alpha_4^2\alpha^2\alpha_5^2 + 6\alpha_4 - 3\alpha_4^4\alpha_5^2 - 3\alpha_4^2\alpha_5^4 - 6\alpha_4^3\alpha_4^3 - 3\alpha_4^2\alpha_5^4 - 3\alpha_5^4\alpha_4^2 - 6\alpha_4^3\alpha_5^2 - 3\alpha_4^2\alpha_5^4 - 3\alpha_4^4\alpha_5^2 + 30\alpha_4^2\alpha_5 q\alpha_5 + 30\alpha_4\alpha_5^2 q\alpha_5 + 60\alpha_4\alpha_5 q\alpha_5^2 - 72\alpha_4\alpha_4\alpha_5 q_1 + 24\alpha_4^2\alpha_5^2 q + 30\alpha_4\alpha_5 q^2 - 6\alpha_4^3\alpha_5 q - 6\alpha_4\alpha_5^3 q + 6q\alpha_4^2\alpha_4^2 - 6q\alpha_5\alpha_4^3 + 24q\alpha_5^3\alpha_4 + 6q\alpha_5^2\alpha_5^2 - 6q\alpha_5\alpha_5^3 + 24q\alpha_5^3\alpha_5 + 24q^2\alpha_5\alpha_4 + 24q^2\alpha_5\alpha_5 - 18\alpha_4^2\alpha_5 q_1 - 18\alpha_4\alpha_5^2 q_1 - 54q\alpha_4 q_1 - 54q\alpha_5 q_1 - 108\alpha_5 q q_1 + 18\alpha_5\alpha_4^3 q_1 - 18\alpha_5^3\alpha_4 q_1 + 18\alpha_5\alpha_5^3 q_1 - 18\alpha_5^2\alpha_5 q_1 + 12q^3 + 12q\alpha_5^4 - 3q^2 - 3q^2\alpha_5^2 + 24q^2\alpha_5^2 + 81q_1^2 + 12q_1\alpha_4^3 + 12q_1\alpha_5^3 - 12q_1\alpha_5^3))^{1/2})^{1/3},$$

$$B = \frac{1}{9}\left(\alpha_4\alpha_5 + 3q - \alpha_5\alpha_4 - \alpha_5\alpha_5 - \alpha_4^2 - \alpha_5^2 - \alpha_5^2\right),$$

$$C = \frac{1}{3}\left(\alpha_4 + \alpha_5 - \alpha_5\right)$$

3.4. Phase Plane Analysis

To obtain the phase portrait of (3.3) we shall use maple 13 package to visualize the complete phase portrait, we need the DETOOL package for differential equation:
The trajectory can be drawn in the phase plane with the phase portrait command:

3.5. Numerical Solution

Since, we won't be able to find solution of the model explicitly as a function of time; we will be solving the system numerically.

We assign some values for k = 0.001, 0.05 and 0.2 respectively while the other parameter remains constant, we also assigned values for d = 0.04, 0.06 and 0.2 respectively while the other parameters remain constant, and r_e = 0.03, 0.19 and 0.3 respectively while the other parameters remain constant and define the system of differential equation. The computations were done using the computer symbolic algebraic package MAPLE

4.0. Results

In this section, we present our results in graphical forms.

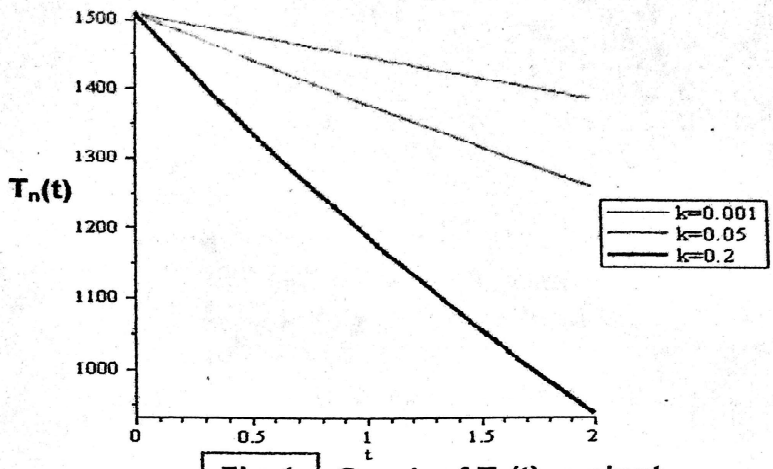

Fig. 1.: Graph of $T_n(t)$ against time (t) for equation (2.2) for different values of k with S_n=0.073, r_c=0.03, d=0.04, η =100, C[max]=300000.

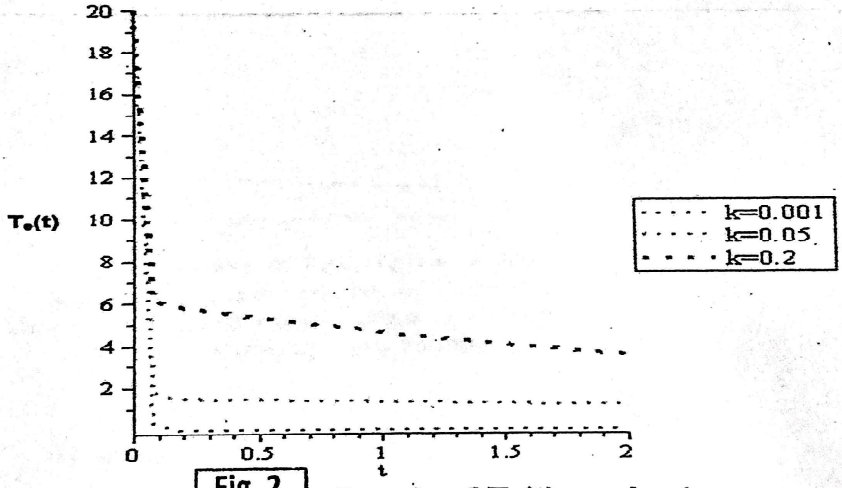

Fig. 2: Graph of $T_e(t)$ against time (t) for equation (2.2) for different values of k with S_n=0.073, r_c=0.03, d=0.04, η =100, C[max]=300000.

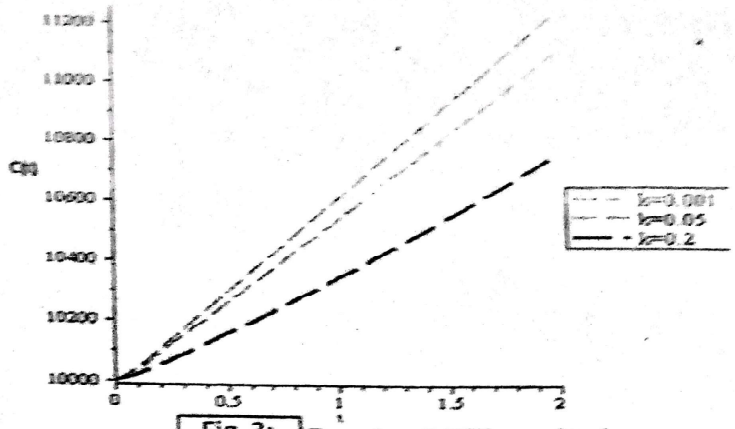

Fig. 3: Graph of C(t) against time (t) for equation (2.2) for different values of k with S_n=0.073, r_c=0.03, d=0.04, η =100, C[max]=300000.

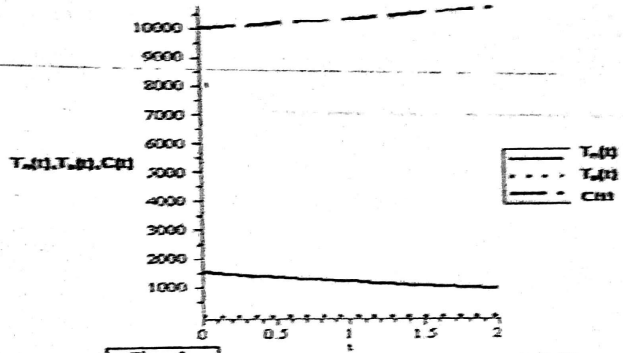

Fig. 4: Graph of $T_n(t)$, $T_e(t)$ and C(t) against time (t) for equation (2.2) for different values of k with S_n=0.073, r_c=0.03, d=0.04, η =100, C[max]=300000.

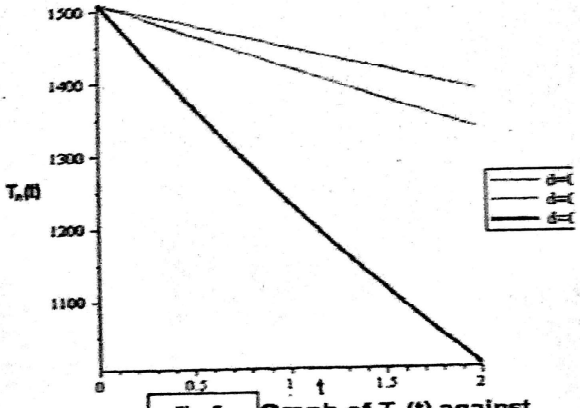

Fig. 5: Graph of $T_n(t)$ against time (t) for equation (2.2) for different values of d with S_n=0.073, r_c=0.03, k=0.001, η =100, C[max]=300000.

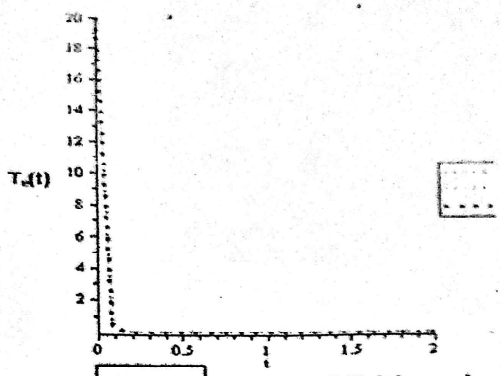

Fig. 6: Graph of $T_R(t)$ against time (t) for equation (2.2) for differ values of d with S_n=0.073, r_c=0.0

k=0.01, η =100, C[max]=300000

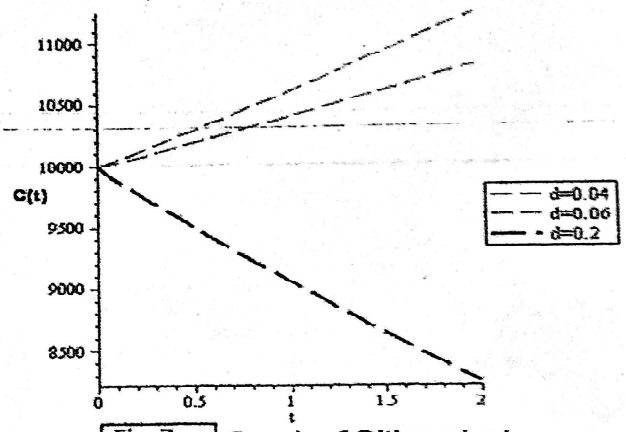

Fig. 7: Graph of C(t) against time (t) for equation (2.2) for different values of d with S_n=0.073, r_c=0.03,

k=0.001, η=100, C[max]=300000.

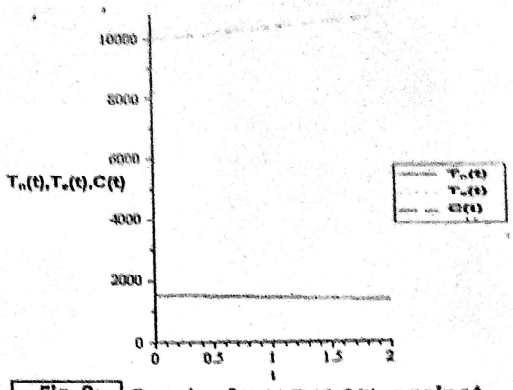

Fig. 8: Graph of $T_n(t),T_e(t),C(t)$ against time (t) for equation (2.2) for different values of d with S_n=0.073, r_c=0.03, k=0.001, η=100, C[max]=300000.

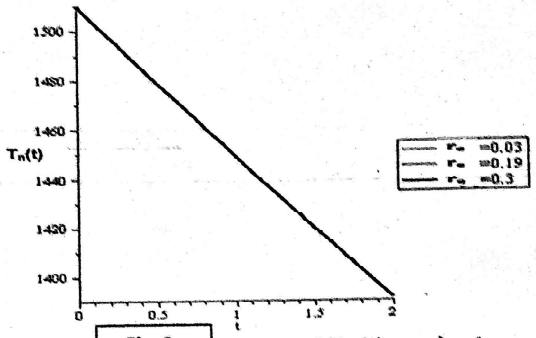

Fig. 9: Graph of T_n (t) against time (t) for equation (2.2) for different values of r_c with S_n=0.073, d=0.04, k=0.001, η=100, C[max]=300000.

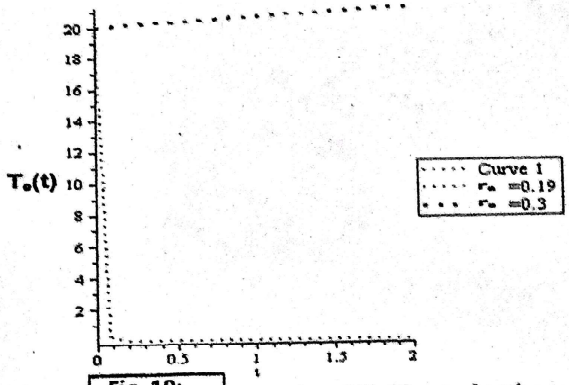

Fig. 10: Graph of T_e(t) against time (t) for equation (2.2) for different values of r_c with S_n=0.073, d=0.04, k=0.001, η=100, C[max]=300000.

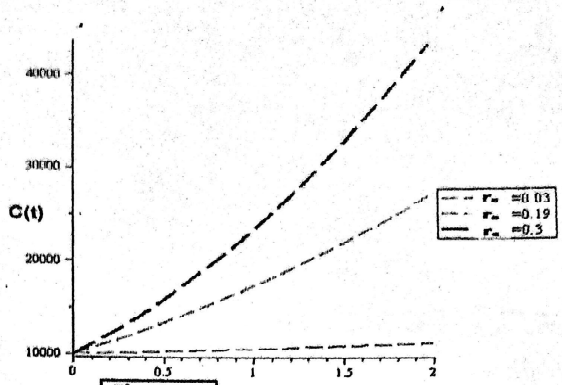

Fig. 11: Graph of C(t) against time (t) for equation (2.2) for different values of r_c with S_n=0.073, d=0.04, k=0.001, η=100, C[max]=300000.

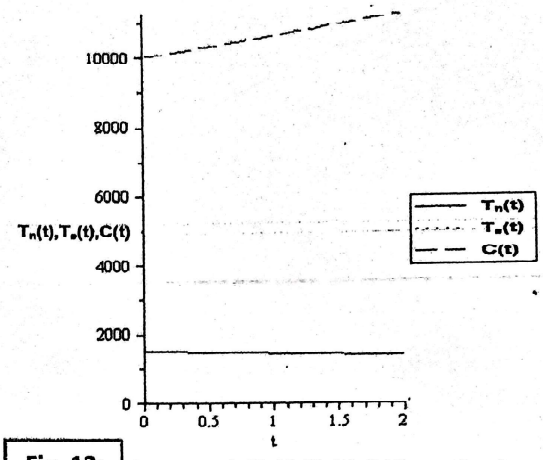

Fig. 12: Graph of $T_n(t)$,$T_e(t)$,C(t) against time (t) for equation (2.2) for different values of r_c with S_n=0.073, d=0.04, k=0.001, η=100, C[max]=300000.

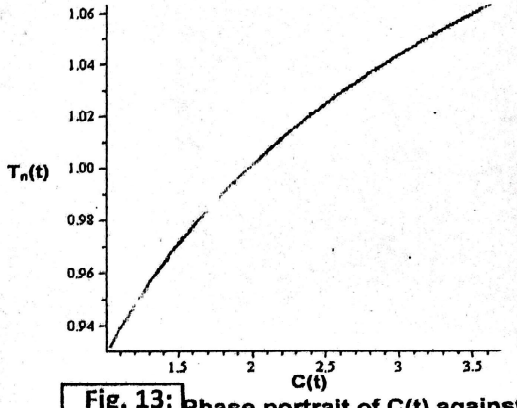

Fig. 13: Phase portrait of C(t) against $T_n(t)$ for equation (2.2) with S_n=0.073, r_c=0.03, d=0.04, k=0.001, γ=0.005, η=100, C[max]=300000.

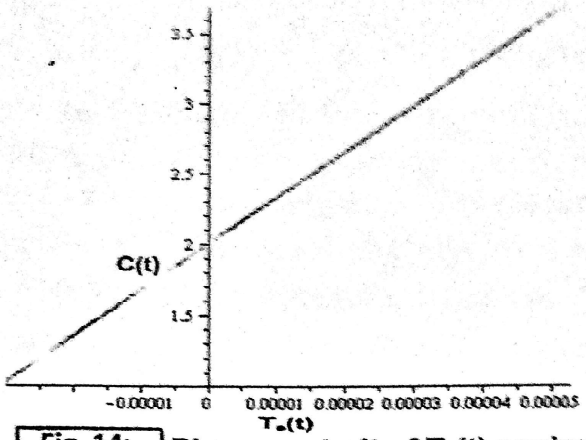

Fig. 14: Phase portrait of $T_e(t)$ against C(t) for equation (2.2) with S_n=0.073, r_c=0.03, d=0.04, k=0.001, γ=0.005, η=100, C[max]=300000.

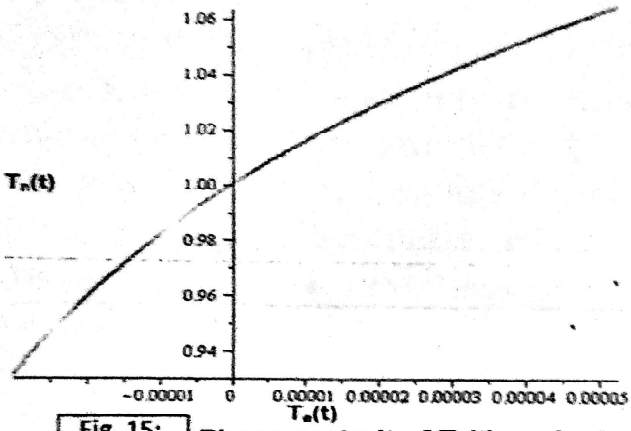

Fig. 15: Phase portrait of $T_e(t)$ against $T_n(t)$ for equation (2.2) with S_n=0.073, r_c=0.03, d=0.04, k=0.001, γ=0.005, η=100, C[max]=300000.

5.0. Discussion of Results

Figure 1 displays the graph of $T_n(t)$ against t for different values of k. We observed that the naive T cells decreases as the activation rate increases. Figure.2 displays the graph of $T_e(t)$ against t for different values of k. We observed that the Effector T cells specific to CML increases as the activation rate increases. Figure 3 displays the graph of $C(t)$ against t for different values of k. We observed that the Chronic Myeloid Leukemia cancer cells increases as the activation rate increases. Figure 4 displays the graph of $T_n(t), T_e(t)$ and $C(t)$ against t for fixed values of parameters. This shows the interaction between the three cell populations. Figure 5 displays the graph of $T_n(t)$ against t for different values of d We observed that the naive T cells decreases as the death rate of the cell populations increases. Figure 6 displays the graph of $T_e(t)$ against t for different values of d. We observed that the Effector T cells specific to CML decreases as the death rate of the cell populations increases. Figure 7 displays the graph of $C(t)$ against t for different values of d. We observed that the Chronic Myeloid Leukemia cancer cells decreases as the death rate of the cell populations increases. Figure 8 displays the graph of $T_n(t), T_e(t)$ and $C(t)$ against t for fixed values of parameters. This shows the interaction between the three cell populations. Figure 9 displays the graph of $T_n(t)$ against t for different values of r_c we observed that the naive T cells decreases as the Contribution due to the growth of C in the form of a Gompertz law increases. Figure 10 displays the graph of $T_e(t)$ against t for different values of r_c. We observed that the Effector T cells specific to CML increases as the Contribution due to the growth of C in the form of a Gompertz law increases. Figure 11 displays the graph of $C(t)$ against t for different values of d. We observed that the Chronic Myeloid Leukemia cancer cells increases as the Contribution due to the growth of C in the form of a Gompertz law increases. Figure 12 displays the graph of $T_n(t), T_e(t)$ and $C(t)$ against t for fixed values of parameters. This shows the interaction between the three cell populations. The phase portraits were presented in Figures 13-15. Figure 13 displays the phase portrait of the number of naïve T cells $T_n(t)$ against the number of chronic myeloid leukemia (CML) cancer cells $C(t)$ for certain values of parameters. Figure 14 displays the phase portrait of the number of chronic myeloid leukemia (CML) cancer cells $C(t)$ against the number of naïve T cells $T_n(t)$ for certain values of parameters. Figure 15 displays the phase portrait of the number of naïve T cells $T_n(t)$ against the number of effector T cells specific to CML $T_e(t)$ for certain values of parameters.

6.0. Conclusions

The most striking observation is that the growth rate of CML r_c, and the natural death rate d, are the most important parameters in the control of CML in this model. The importance of r_c suggest that Gleevec and other drugs which attempt to block excessive growth rate of CML are likely to be successful treatments for CML, for the duration of their effectiveness. Our results also give some indication that increasing d may not be sufficient in all cases in controlling CML, which matches observation of current treatments, and which we hope will be investigated more closely by other researchers. Chronic myeloid leukemia (CML)

is a rare type of blood cancer that typically grows worse slowly but is gradually doing havoc to the human population. To this effect, adequate measures should be put into consideration to put a stop to this life threatening disease that is creeping into the human race. Therefore, we strongly recommend that programmes like the Gleevec International Patient Assistance Program (GIPAP) be set up between a manufacturer (Navatis) and an NGO (The max foundation) to provide free treatment to eligible CML patients in Nigeria. We further recommend that this research work be improved by other researchers in the field of mathematics to bring up effective strategies that will assist the federal government to look into the control measures to be implemented.

References

Akinwande N. I. (2009). Study of the Contribution of Prof C.O.A Sowunmi in the Field of Biomathematics Using Deterministic Mathematical Models of Population Dynamics. *Advances in Mathematics* 1 (1), 1-12, Ibadan, Nigeria.

Angstreich G., Smith B., and Jones, R. (2004). Treatment Options for Chronic Myelogenous Leukemia: Imatinib Versus Interferon Versus Allogeneic Transplant. *Curr. Opin. Oncol.*, *16*, 95–99.

Bruce A., Dennis B., Julian L, Martin R., Keith R., and James D.W. (1994). " *Molecular Biology of the Cell"*. Garland Publishing, Inc.

Cortes J., Talpaz M., O'Brien S., Jones D., Luthra R. (2005). Molecular Responses in Patients with Chronic Myelogenous Leukemia in Chronic Phase Treated with Imatinib Mesylate. *Clin. Cancer Res.*, *11*, 3425–3432.

Faderl S., Talpaz M., Estrov Z., Kantarjian H.M. (1999). Chronic Myelogenous Leukemia: Biology and Therapy. *Annals of Internal Medicine* 131 (3): 207–219. PMID 10428738.

Leukemia & Lymphoma Society 2012 annual report (2012) www.lls.org/content/nationalcontent/pdf/**2012**annualreport.pdf

Moloney W.C. (1987). Radiogenic Leukemia Revisited. *Blood* 70 (4): 905–8. PMID 3477299.

Shapira T., Pereg D., Lishner M. (2008). "How I treat acute and chronic leukemia in pregnancy". *Blood Rev.* **22** (5): 247–59. doi:10.1016/j.blre.2008.03.006. PMID 18472198.

Schiffer C.A., Hehlmann, R., Larson, R. (2003). Perspectives on the Treatment of Chronic Phase and Advanced Phase CML and Philadelphia Chromosome Positive ALL. Leukemia 17, 691–699.