MATHEMATICAL MODELLING OF TUBERCULOSIS-COVID-19 CO-INFECTION

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DECLARATION

This project is my original work and has not been presented for a degree or other award in any other university.

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DEDICATION

This work is dedicated to God Almighty.

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NOMENCLATURE

Symbol	Meaning
S	Susceptible compartment
C	COVID-19 infected compartment
T	Tuberculosis infected compartment
Λ	Influx rate into the susceptible population
α_1	Recruitment rate into C
α_2	Recruitment rate into T
r_1	Recovery rate of C
r_2	Recovery rate of T
r_3	Recovery rate of I
d_1	COVID-19-induced death rate
d_2	Tuberculosis-induced death rate
I	Co-infected compartment
R	Recovered compartment
β_1	Rate at which members of C get co-infected with tuberculosis
β_2	Rate at which members of T get co-infected with COVID-19
ϵ	Rate at which R losses its immunity
μ	Natural death rate

ABSTRACT

It was noted that the spread of tuberculosis reduced significantly during the COVID-19 pandemic. This reduction has been associated with the preventive measures placed to combat the spread of COVID-19. Research showed a strong correlation between the spread of COVID-19 and the spread of tuberculosis in any population. It is worth noting that tuberculosis and COVID-19 are among the leading most deadly communicable diseases in the world today. The correlation in their spread also leaves us to believe that the spread of one can enhance the spread of the other. Hence, we proposed a situation where a population was co-infected with both COVID-19 and tuberculosis. By employing the conservative laws, the mathematical model was formulated, and the resulting model analysed both qualitatively and numerically. The equilibrium points of the model were obtained and the reproduction number calculated. The condition for stability of the co-infection at the equilibrium point was determined as $R_0 < 1$. The non-negativity conditions for the solution were established. A numerical simulation was carried out for the model and the dynamics of the diseases studied as the parameters vary. It was found that the rate of contracting tuberculosis posessed a more significant impact on the possibility of coinfection than COVID-19 and the effects of migration from the tuberculosis sub-population were more significant than migration from COVID-19.

1

INTRODUCTION

1.1 Background Information

COVID-19, a short form of coronavirus disease that spiked into a pandemic in 2019, was caused by SARS-CoV-2, originating from Wuhan, China. The coronavirus is a virus family that originated in animals but has been discovered to infect humans with respiratory diseases. They were not considered fatal until COVID-19 evolved, which has claimed the lives of over 6 million people globally. Although the first instance was reported in Wuhan, China, it is still unknown how the sickness was transmitted to humans. However, it is thought that the disease originated in bats or wolf pulps (Toit, 2020). Ever since the entrance of the virus into one human from an unknown origin, it has since spread from human to human. The spread happens by contaminated droplets when infected people sneeze, or cough (Seifirad, 2020; Bada *et al.*, 2021). Symptoms of infection include high fever, breath shortness, cough, and running nose. Symptoms begin to appear within fourteen days from the day of infection (Horowitz and Freeman, 2020; Kumar Raghav and Mohanty, 2020).

Tuberculosis is a bacterial infection caused by the mycobacterium tuberculosis. It is an infection of the lungs, kidney and spine that is transmitted via droplets from infected individuals. The infection is in two phases; the latent phase and the active phase (Nainggolan *et al.*, 2013). The latent phase of the tuberculosis infection is not harmful to the body and produces no symptoms but the active phase becomes a major sickness after months or years of infection (Okuonghae and Ikhimwin, 2016; Kabunga *et al.*, 2020).

COVID-19 disease presence in an individual makes the individual vulnerable to tuberculosis while the presence of tuberculosis makes the individual vulnerable to COVID-19. Hence, one of the diseases can come as a secondary infection when an individual is infected with the other. COVID-19 has claimed the lives of around 6.32 million human beings globally since 2019 (Juma et al., 2024) and it is classified as the most deadly infectious disease globally (Oke et al., 2022). Tuberculosis is the next in line, killing over 1.5 million individuals in 2020. This shows the threat posed to an individual if they are co-infected with both COVID-19 and tuberculosis (CDC, 2020). Equipped with these pieces of information, it becomes very pertinent to examine the flow of COVID-19/tuberculosis co-infection in a population. A mathematical model to examine the COVID-19/tuberculosis co-infection dynamics in any population is investigated in this study. The qualitative analysis of the model is carried out to establish the conditions for the stability of the solution. By simulating the model for various parameter values, the variation of COVID-19/tuberculosis co-infection in a given population is investigated.

1.2Statement of the Problem

An individual infected with COVID-19 disease is prone to tuberculosis and vice versa. The fact that either of the diseases can come as an opportunistic infection once the other has infected the host necessitates the study of co-infection of both tuberculosis and COVID-19. This study investigates the COVID-19/tuberculosis co-infection dynamics in a population. A deterministic mathematical model is formulated to explain the trend in the COVID-19/ tuberculosis co-infection.

1.3Objectives

1.3.1General objective

This research aims to investigate the trend of COVID-19/tuberculosis co-infection in a given population.

1.3.2Specific objectives

The following specific objectives are pursued;

i To formulate the mathematical model for the COVID-19/tuberculosis co-infection.

ii To determine the region of the solution and the non-negativity of the solution.

iii To simulate the model inorder to investigate the dynamics of the COVID-19/tuberculosis co-infection.

1.4Justification of the Study

The social nature of human beings makes the human population vulnerable to the rapid spread of infectious diseases. COVID-19 and tuberculosis are the two leading most deadly infectious diseases. It is alarming to observe that over 2 million deaths were related to COVID-19 in 2020 and over 1.5 million deaths were related to tuberculosis in 2020. This indicates the possible fatality embedded in the simultaneous existence of both diseases in a population. Hence, this research focuses on COVID-19/tuberculosis co-infection dynamics in a population.

1.5Significance of the Study

The preventive measures set against COVID-19 are also good measures to achieve a reduction in tuberculosis cases. Meanwhile, if the two diseases should hit a certain population at the same time, it appears the population will be badly affected. In lieu of this, this study considers the trend when there is COVID-19/tuberculosis co-infection. The simulations from this study shall provide a trend to expect in any case that a population is hit by the COVID-19/tuberculosis co-infection. In addition, the outcome of this research provides significance for further research.

2

LITERATURE REVIEW

The emergence of COVID-19 in 2019 brought about a paradigm shift in many facets of human endeavours. The mortality rate was very high and it became the most deadly disease in 2020. It is also important to note that despite the enormous resources directed into research on COVID-19, little progress has been made to unravel the mysteries surrounding the disease. The rapid evolution and mutation of COVID-19 make it difficult for scientists to come up with a cure. In the least, vaccines have been developed to prevent infection with COVID-19 (Li *et al.*, 2021). Tuberculosis on the other hand has been around for decades but it has not been considered as a global pandemic despite claiming more lives than 90% of other infectious diseases. Tuberculosis has been given less attention than it deserves in this past decade and Bates and Stead (1993) advocated that tuberculosis should be named a global epidemic. Bates and Stead (1993) pointed out that the duration of tuberculosis in a population is an important factor in properly understanding the trend in the population.

Mathematical modelling provides scientists with a very economical approach to studying the trend of an epidemic. The disease and its trend can be studied before it hits the population and vital recommendations can be made even before the disease hits the population. In the case of COVID-19, scientists were quick to formulate mathematical models for the transmission of the disease. Aldila *et al.* (2020) proposed a model for investigating the effects of social distancing in a bid to control the COVID-19 spread, with an emphasis on prompt testing. Annas *et al.* (2020) adopted a mathematical model for studying the COVID-19 spread in Indonesia. Oke *et al.* (2021) studied the possibility of re-infection, relapse or recurrence of COVID-19 in recovered individuals. Wangari *et al.* (2021) included the hospitalised compartment, contact tracing, and testing in large groups on the impact of reinfection of COVID-19 in the mathematical modelling of the trend of COVID-19 in Kenya.

Mathematical modelling of infectious diseases is not limited to COVID-19 spread, various researchers have considered modelling of tuberculosis and its spread. Okuonghae and Ikhimwin (2016) analysed the effect of awareness on the progression of tuberculosis by using the compartmentalised model system. The study proposed that concentration should be placed on awareness programmes. A further study was carried out by Chong *et al.* (2019) to predict the influence of early detection and treatment of latent tuberculosis on the vulnerable group of the elderly. A recommendation to closely monitor the latent tuberculosis treatment in the elderly was raised. Fatmawati *et al.* (2020) advocated for the use of fractional calculus in mathematical modelling due to its ability to investigate the salient properties of the mathematical model. The study considered the two vulnerable groups of the elderly and children and the results indicated that infected individuals increase with increasing fractional order. The mathematical model formulated by Ayinla *et al.* (2021) was used to predict the tuberculosis epidemic and they found that lowering the rate of vaccination gives tuberculosis a higher chance of persisting in any population.

Recently, Mekonen *et al.* (2022) had considered the possibility of tuberculosis/COVID-19 co-infection. The study proposed an 8-compartment mathematical model in which the recovered compartment is considered as an absorbing state. This study aims at modifying the work of Mekonen *et al.* (2022). It is interesting to observe that some of the 8 compartments proposed by Mekonen *et al.* (2022) can be merged into a single compartments. The latent stage of tuberculosis and COVID-19 can be merged into a single compartment. Also, Mekonen *et al.* (2022) had considered the recovered compartment as an absorbent state, whereas it has been recorded by Oke *et al*. (2021) that relapse and reinfection are possible. Hence, this study proposes a 5-compartment mathematical model to investigate the COVID-19/tuberculosis co-infection dynamics.

3

METHODOLOGY

3.1Introduction

A mathematical model that considers the dynamics of the individuals who get co-infected with both tuberculosis and COVID-19 is formulated in this section. The population is compartmentalised into five groups: susceptible group S, COVID-19 infected group C, Tuberculosis infected group T, COVID-19 and tuberculosis co-infected group I, and Recovered group R. The susceptible group is the part of the population who possess a chance of contracting either COVID-19 or tuberculosis. Individuals who have COVID-19 only are classed into the COVID-19 infected group, individuals who are infected with tuberculosis only are classed into the tuberculosis group and individuals who have both COVID-19 and tuberculosis are classed in the Infected group. The recovered class consists of all individuals who have been cured of any of the diseases. The model is formulated built on the following assumptions;

i Every member of the population gives birth to healthy children (i.e. without tuberculosis or COVID-19).

ii Tuberculosis and COVID-19 are transmitted by interaction with infected individuals.

iii Individuals infected with either tuberculosis or COVID-19 or both either recover or die.

iv Individuals from each compartment can die a natural death.

In subsequent sections, the reproduction numbers for the co-infection are obtained using the next-generation matrix (NGM) for the mathematical model. The non-negativity conditions are established for the model and the stability of the equilibrium points are also obtained.

3.2Model Formulation

Individuals born into the population are born without tuberculosis or COVID-19 and there is a constant influx into the population at the rate Λ. Susceptible individuals get COVID-19 at the rate α_1 when they interact with individuals carrying COVID-19. Also, a susceptible individual gets infected with tuberculosis at a rate α_2 when they interact with tuberculosis-infected individuals. The COVID-19-infected individuals who interacted with tuberculosis patients also get tuberculosis at the rate of β_1 while tuberculosis-infected individuals who interacted with COVID-19-infected also get COVID-19 at the rate of β_2. The rates at which individuals infected with COVID-19 only, tuberculosis only, and co-infected with both diseases recover from their infections are r_1, r_2, r_3 respectively. Individuals from the population die a natural death at the rate μ, COVID-19-induced deaths occur at the rate d_1, tuberculosis-induced deaths occur at the rate d_2. Figure 3.1 shows the pictorial representation.

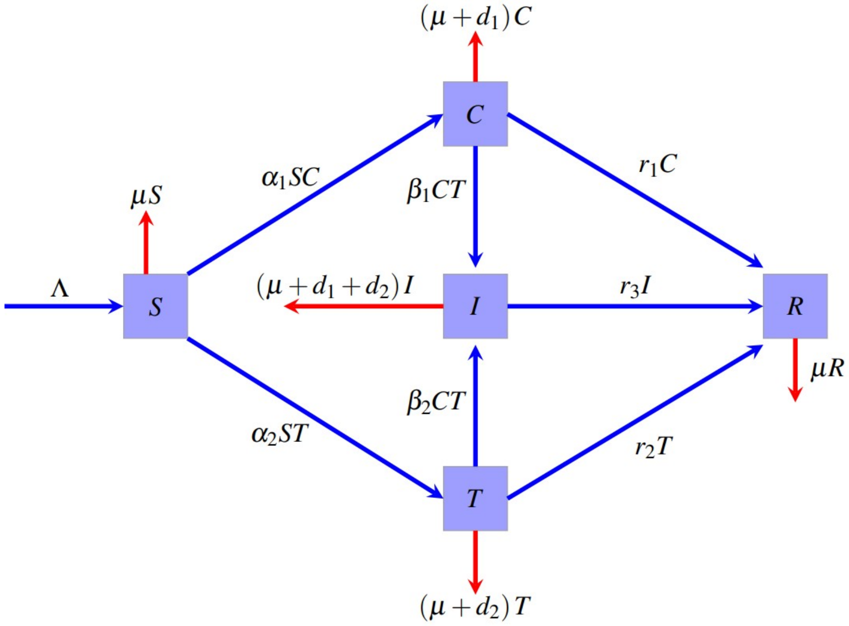


Figure 3.1: Spread configuration

The dynamics of co-infection of both COVID-19 and tuberculosis described so far are modelled into the system of equations;

$$\frac{dS}{dt} = \Lambda - \mu S - \alpha_1 SC - \alpha_2 ST \,, \tag{3.2.1}$$

$$\frac{dC}{dt} = \alpha_1 SC - \beta_1 CT - (\mu + d_1) C - r_1 C \,, \tag{3.2.2}$$

$$\frac{dT}{dt} = \alpha_2 ST - \beta_2 CT - (\mu + d_2) T - r_2 T \,, \tag{3.2.3}$$

$$\frac{dI}{dt} = \beta_1 CT + \beta_2 CT - (\mu + d_1 + d_2) I - r_3 I \,, \tag{3.2.4}$$

$$\frac{dR}{dt} = r_1 C + r_2 T + r_3 I - \mu R \,. \tag{3.2.5}$$

with the following conditions;

$$0 \leq \mu, \alpha_1, \alpha_2, \beta_1, \beta_2, d_1, d_2, r_1, r_2, r_3, \epsilon \leq 1 \,,$$

and the entire population $N(t)$ is given by

$$N(t) = S(t) + C(t) + T(t) + I(t) + R(t) \,. \tag{3.2.6}$$

Summing up equations (3.2.1) - (3.2.5), we have

$$\frac{d}{dt}(S + C + T + I + R) = \Lambda - \mu (S + C + T + I + R) - d_1 C - d_2 T - (d_1 + d_2) I \,.$$

Using equation (3.2.6), we have

$$\frac{dN}{dt} = \Lambda - \mu N - d_1 C - d_2 T - (d_1 + d_2) I \leq \Lambda - \mu N \,.$$

Hence, by separating the variables, the equation is solved to get

$$N \leq \frac{\Lambda}{\mu} - \left(\frac{\Lambda}{\mu} - N(0) \right) \exp(-\mu t) \,,$$

where $N(0)$ is the initial population. As $t \to \infty$,

$$N \to \frac{\Lambda}{\mu} \,.$$

Hence, the problem is epidemiologically feasible and the solution can be sought in the region

$$R=\left\{(S,C,T,I,R):S+C+T+I+R\leq\frac{\Lambda}{\mu}\right\}.$$

3.3Qualitative Analysis of the Model

The first step in the qualitative analysis is to get the equilibrium points. This is done by setting each of the equations (3.2.1) - (3.2.3) to zero as follows;

$$\Lambda-\mu S-\alpha_1 SC-\alpha_2 ST=0, \tag{3.3.1}$$

$$\alpha_1 SC-\beta_1 CT-(\mu+d_1)C-r_1 C=0, \tag{3.3.2}$$

$$\alpha_2 ST-\beta_2 CT-(\mu+d_2)T-r_2 T=0, \tag{3.3.3}$$

$$\beta_1 CT+\beta_2 CT-(\mu+d_1+d_2)I-r_3 I=0, \tag{3.3.4}$$

$$r_1 C+r_2 T+r_3 I-\mu R=0. \tag{3.3.5}$$

The disease-free equilibrium point (DFE) is obtained in the absence of diseases in the population, that is,

$$C=T=I=0. \tag{3.3.6}$$

Clearly, substituting condition (3.3.6) satisfies equations (3.3.2), (3.3.3) and (3.3.4). Furthermore, putting the condition (3.3.6) into equation (3.3.5) leads to $R=0$. Putting the condition (3.3.6) into the equation (3.3.1) gives

$$\Lambda-\mu S=0\Rightarrow S=\frac{\Lambda}{\mu}.$$

Thus, we have the DFE E_0 as

$$E_0=\left(S_0,C_0,T_0,I_0,R_0\right)=\left(\frac{\Lambda}{\mu},0,0,0\right).$$

The endemic equilibrium point (EEP) is the situation where COVID-19 and tuberculosis remain in the population. From equation (3.3.1),

$$\Lambda-\mu S-\alpha_1 SC-\alpha_2 ST=0$$

$$\Rightarrow \Lambda-\left(\mu+\alpha_1 C+\alpha_2 T\right)S=0,$$

$$\Rightarrow\left(\mu+\alpha_1 C+\alpha_2 T\right)S=\Lambda$$

$$\Rightarrow S^{¿}=\frac{\Lambda}{\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}}. \tag{3.3.7}$$

Summing equations (3.3.2), (3.3.3) and (3.3.4), we have

$$\alpha_1 SC-\left(\mu+d_1+r_1\right)C+\alpha_2 ST-\left(\mu+d_2+r_2\right)T-\left(\mu+d_1+d_2+r_3\right)I=0,$$

$$\left(\alpha_1 C+\alpha_2 T\right)S-\left(\mu+d_1+r_1\right)C-\left(\mu+d_2+r_2\right)T-\left(\mu+d_1+d_2+r_3\right)I=0,$$

$$I=\frac{\left(\alpha_1 C+\alpha_2 T\right)S-\left(\mu+d_1+r_1\right)C-\left(\mu+d_2+r_2\right)T}{\mu+d_1+d_2+r_3}.$$

Substituting $S^{¿}$ gives

$$I^{¿}=\frac{\left(\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)\Lambda-\left(\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)\left(\left(\mu+d_1+r_1\right)C^{¿}-\left(\mu+d_2+r_2\right)T^{¿}\right)}{\left(\mu+d_1+d_2+r_3\right)\left(\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)}.$$

Solving for R in equation (3.3.5) gives

$$r_1 C+r_2 T+r_3 I-\mu R=0\mu R=r_1 C+r_2 T+r_3 I\, R^{¿}=\frac{r_1}{\mu}C^{¿}+\frac{r_2}{\mu}T^{¿}+\frac{r_3}{\mu}I^{¿}$$

Thus the EEP is

$$\left(S^{¿},C^{¿},T^{¿},I^{¿},R^{¿}\right)$$

where

$$S^{¿}=\frac{\Lambda}{\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}},\ R^{¿}=\frac{r_1}{\mu}C^{¿}+\frac{r_2}{\mu}T^{¿}+\frac{r_3}{\mu}I^{¿},$$

$$I^{¿}=\frac{\left(\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)\Lambda-\left(\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)\left(\left(\mu+d_1+r_1\right)C^{¿}-\left(\mu+d_2+r_2\right)T^{¿}\right)}{\left(\mu+d_1+d_2+r_3\right)\left(\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)}.$$

An in-depth understanding of the spread of the diseases can be studied if the reproduction number is known. The reproduction number is denoted as R_0, tracks the new infections brought about by the introduction of one infectious individual into a susceptible population. The next-generation matrix is used to find R_0 by considering the infectious classes (C, T, I) and classifying the new infections into F and the negation of the outward transmission into V, thus

$$F=\begin{pmatrix}\alpha_1 SC\\ \alpha_2 ST\\ \beta_1 CT+\beta_2 CT\end{pmatrix},\ V=\begin{pmatrix}\beta_1 CT+\left(\mu+d_1+r_1\right)C\\ \beta_2 CT+\left(\mu+d_2+r_2\right)T\\ \left(\mu+d_1+d_2+r_3\right)I\end{pmatrix}.$$

It follows that

$$\nabla F=\begin{pmatrix}\alpha_1 S & 0 & 0\\ 0 & \alpha_2 S & 0\\ \beta_1 T+\beta_2 T & \beta_1 C+\beta_2 C & 0\end{pmatrix},\Rightarrow\left(\nabla F\right)_{E_0}=\begin{pmatrix}\frac{\alpha_1 \Lambda}{\mu} & 0 & 0\\ 0 & \frac{\alpha_2 \Lambda}{\mu} & 0\\ 0 & 0 & 0\end{pmatrix}$$

$$\nabla V=\left(\nabla V\right)_{E_0}=\begin{pmatrix}\mu+d_1+r_1 & 0 & 0\\ 0 & \mu+d_2+r_2 & 0\\ 0 & 0 & \mu+d_1+d_2+r_3\end{pmatrix}$$

and

$$(\nabla V)_{E_0}^{-1}=\begin{pmatrix} \frac{1}{\mu+d_1+r_1} & 0 & 0 \\ 0 & \frac{1}{\mu+d_2+r_2} & 0 \\ 0 & 0 & \frac{1}{\mu+d_1+d_2+r_3} \end{pmatrix}.$$

From which

$$(\nabla F)_{E_0}(\nabla V)_{E_0}^{-1}=\begin{pmatrix} \frac{\alpha_1 \Lambda}{\mu(\mu+d_1+r_1)} & 0 & 0 \\ 0 & \frac{\alpha_2 \Lambda}{\mu(\mu+d_2+r_2)} & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

The eigenvalues are found from the equation;

$$\begin{vmatrix} \frac{\alpha_1 \Lambda}{\mu(\mu+d_1+r_1)}-\lambda & 0 & 0 \\ 0 & \frac{\alpha_2 \Lambda}{\mu(\mu+d_2+r_2)}-\lambda & 0 \\ 0 & 0 & -\lambda \end{vmatrix}=0\left(\frac{\alpha_2 \Lambda}{\mu(\mu+d_2+r_2)}-\lambda\right)\left(\frac{\alpha_1 \Lambda}{\mu(\mu+d_1+r_1)}-\lambda\right)\lambda=0,$$

Indicating that the eigenvalues are

$$\lambda_1=\frac{\alpha_1 \Lambda}{\mu(\mu+d_1+r_1)},\lambda_2=\frac{\alpha_2 \Lambda}{\mu(\mu+d_2+r_2)},\lambda_3=0$$

Finally, the basic reproduction number is

$$R_0=max\{\lambda_1,\lambda_2,\lambda_3\}=max\left\{\frac{\alpha_1 \Lambda}{\mu(\mu+d_1+r_1)},\frac{\alpha_2 \Lambda}{\mu(\mu+d_2+r_2)},0\right\}.$$

Theorem 3.3.1: *The DFE is locally asymptotically stable if* $R_0<1$.

Proof. The Jacobian matrix for the system (3.2.1 to 3.2.3) is

$$J=\begin{pmatrix} -(\mu+\alpha_1 C+\alpha_2 T) & -\alpha_1 C & -\alpha_2 S & 0 & 0 \\ \alpha_1 C & \alpha_1 S-\beta_1 T-(\mu+d_1+r_1) & -\beta_1 C & 0 & 0 \\ \alpha_2 T & -\beta_2 T & \alpha_2 S-\beta_2 T-(\mu+d_2+r_2) & 0 & 0 \\ 0 & \beta_1 T+\beta_2 T & \beta_1 C+\beta_2 C & -(\mu+d_1+d_2+r_3) & 0 \\ 0 & r_1 & r_2 & r_3 & -\mu \end{pmatrix}.$$

When we substitute the DFE, we get

$$J=\begin{pmatrix} -\mu & 0 & -\alpha_2\frac{\Lambda}{\mu} & 0 & 0 \\ 0 & \frac{\alpha_1 \Lambda}{\mu}-(\mu+d_1+r_1) & 0 & 0 & 0 \\ 0 & 0 & \frac{\alpha_2 \Lambda}{\mu}-(\mu+d_2+r_2) & 0 & 0 \\ 0 & 0 & 0 & -(\mu+d_1+d_2+r_3) & 0 \\ 0 & r_1 & r_2 & r_3 & -\mu \end{pmatrix}.$$

The characteristic equation therefore gives

$$\begin{vmatrix} -\mu-\lambda & 0 & -\alpha_2\frac{\Lambda}{\mu} & 0 & 0 \\ 0 & \frac{\alpha_1 \Lambda}{\mu}-(\mu+d_1+r_1)-\lambda & 0 & 0 & 0 \\ 0 & 0 & \frac{\alpha_2 \Lambda}{\mu}-(\mu+d_2+r_2)-\lambda & 0 & 0 \\ 0 & 0 & 0 & -(\mu+d_1+d_2+r_3)-\lambda & 0 \\ 0 & r_1 & r_2 & r_3 & -\mu-\lambda \end{vmatrix}=0.$$

Taking the determinant along the last row and last column, we have

$$(-\mu-\lambda)\begin{vmatrix} -\mu-\lambda & 0 & -\alpha_2\frac{\Lambda}{\mu} & 0 \\ 0 & \frac{\alpha_1 \Lambda}{\mu}-(\mu+d_1+r_1)-\lambda & 0 & 0 \\ 0 & 0 & \frac{\alpha_2 \Lambda}{\mu}-(\mu+d_2+r_2)-\lambda & 0 \\ 0 & 0 & 0 & -(\mu+d_1+d_2+r_3)-\lambda \end{vmatrix}=0.$$

Again, taking the determinant along the last row and last column, we have

$$(-\mu-\lambda)\left(-(\mu+d_1+d_2+r_3)-\lambda\right)\begin{vmatrix} -\mu-\lambda & 0 & -\alpha_2\dfrac{\Lambda}{\mu} \\ 0 & \dfrac{\alpha_1\Lambda}{\mu}-(\mu+d_1+r_1)-\lambda & 0 \\ 0 & 0 & \dfrac{\alpha_2\Lambda}{\mu}-(\mu+d_2+r_2)-\lambda \end{vmatrix}=0$$

Taking the determinant along the last row and last column one more time, we have

$$(-\mu-\lambda)\left(-(\mu+d_1+d_2+r_3)-\lambda\right)\left(\frac{\alpha_2\Lambda}{\mu}-(\mu+d_2+r_2)-\lambda\right)\begin{vmatrix} -\mu-\lambda & 0 \\ 0 & \dfrac{\alpha_1\Lambda}{\mu}-(\mu+d_1+r_1)-\lambda \end{vmatrix}=0$$

and finally

$$(-\mu-\lambda)\left(-(\mu+d_1+d_2+r_3)-\lambda\right)\left(\frac{\alpha_2\Lambda}{\mu}-(\mu+d_2+r_2)-\lambda\right)\left(\frac{\alpha_1\Lambda}{\mu}-(\mu+d_1+r_1)-\lambda\right)(-\mu-\lambda)=0$$

which means

$$\lambda_1=-\mu,\lambda_2=-(\mu+d_1+d_2+r_3),\lambda_3=\frac{\alpha_2\Lambda}{\mu}-(\mu+d_2+r_2),$$

$$\lambda_4=\frac{\alpha_1\Lambda}{\mu}-(\mu+d_1+r_1),\lambda_5=-\mu.$$

All eigenvalues are negative only if

$$\frac{\alpha_2\Lambda}{\mu}-(\mu+d_2+r_2)<0,(for\ \lambda_3<0)\Rightarrow\frac{\alpha_2\Lambda}{\mu}<(\mu+d_2+r_2)\Rightarrow\frac{\alpha_2\Lambda}{\mu(\mu+d_2+r_2)}<1,$$

and

$$\frac{\alpha_1\Lambda}{\mu}-(\mu+d_1+r_1)<0,(for\ \lambda_4<0)\Rightarrow\frac{\alpha_1\Lambda}{\mu}<(\mu+d_1+r_1)\Rightarrow\frac{\alpha_1\Lambda}{\mu(\mu+d_1+r_1)}<1\Rightarrow R_0<1.$$

4

DISCUSSION OF RESULTS

4.1Model Solution

The numerical method adopted in solving the model is the Runge-Kutta method of order 4 (Oke, 2017). Given a system of differential equations

$$\dot{X}=G(t,X)$$

for some vector variable X, the Runge-Kutta scheme of the order 4 is as follows ;

$$K_1=hG(t,X_n),K_2=hG\left(t+\frac{h}{2},X_n+\frac{1}{2}K_1\right),K_3=hG\left(t+\frac{h}{2},X_n+\frac{1}{2}K_2\right),K_4=hG(t+h,X_n+K_3)$$

and the updated solution at the next time step $n+1$ is

$$X_{n+1}=X_n+\frac{1}{6}(K_1+2K_2+2K_3+K_4).$$

The model (3.2.1 to 3.2.6) is an autonomous equation since the right-hand side of all equations is not explicitly dependent on time and the Runge-Kutta scheme becomes

$$K_1=hG(X_n)K_2=hG\left(X_n+\frac{1}{2}K_1\right)K_3=hG\left(X_n+\frac{1}{2}K_2\right)K_4=hG(X_n+K_3)$$

with

$$X_{n+1}=X_n+\frac{1}{6}(K_1+2K_2+2K_3+K_4),$$

where

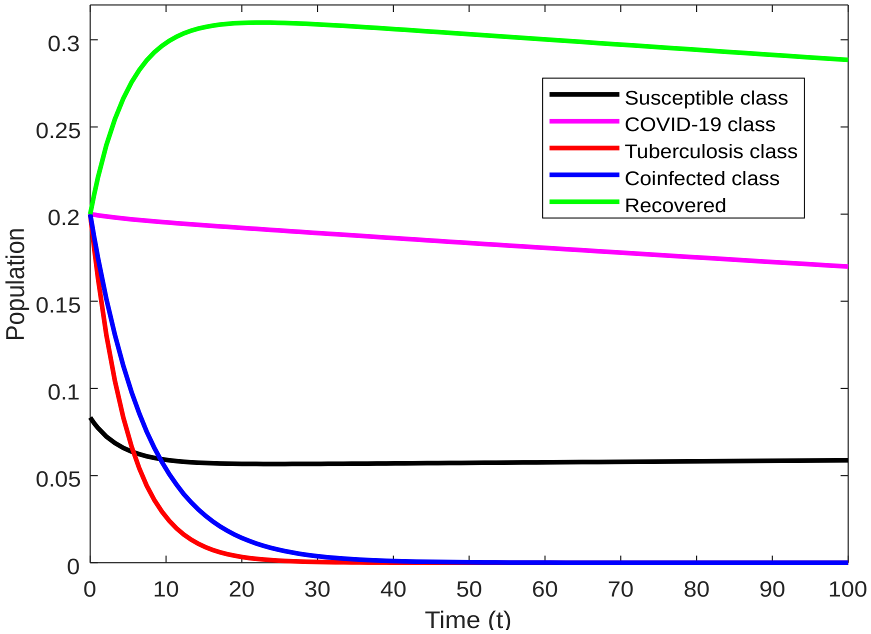
$$X_n=\begin{pmatrix}S_n\\C_n\\T_n\\I_n\\R_n\end{pmatrix},G(X_n)=\begin{pmatrix}\Lambda-\mu S_n-\alpha_1 S_n C_n-\alpha_2 S_n T_n\\\alpha_1 S_n C_n-\beta_1 C_n T_n-(\mu+d_1)C_n-r_1 C_n\\\alpha_2 S_n T_n-\beta_2 C_n T_n-(\mu+d_2)T_n-r_2 T_n\\\beta_1 C_n T_n+\beta_2 C_n T_n-(\mu+d_1+d_2)I_n-r_3 I_n\\r_1 C_n+r_2 T_n+r_3 I_n-\mu R_n\end{pmatrix}$$

It is worth noting that there are 11 parameters whose values are obtained from literature or by estimation. The parameters pertaining to tuberculosis and its spread can be found in Das *et al.* (2021) while the parameters pertaining to COVID-19 spread can be found in Oke *et al.* (2021). The choices of the parameter values are as follows;

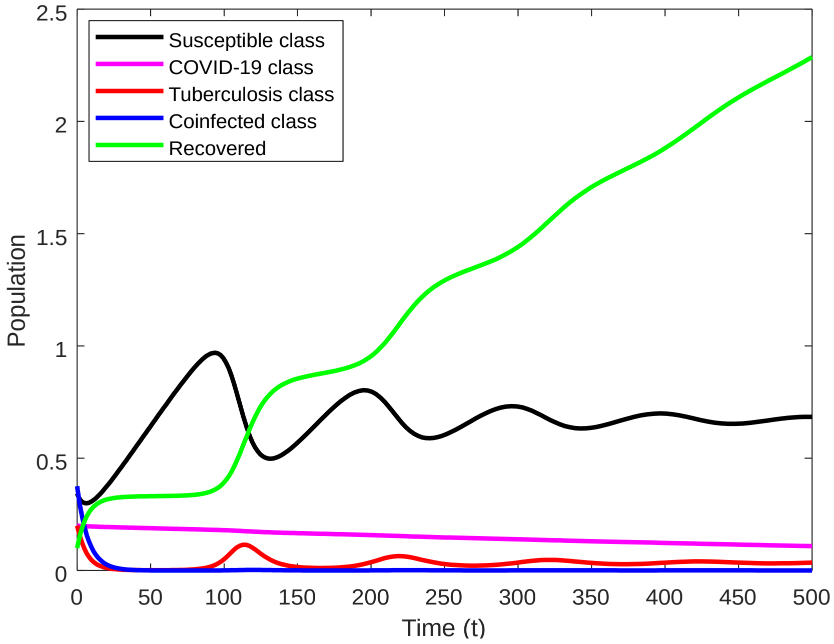
$$\Lambda=0.0001\,;\mu=0.0012\,;\alpha_1=0.000085044\,;\alpha_2=0.4048\,;\beta_1=0.01\,;$$

$$\beta_2=0.01\,;d_1=2.51357e-6\,;d_2=2.51357e-6\,;r_1=0.000334287\,;r_2=0.104\,;r_3=0.01\,.$$

By varying the values of the parameters, we solve the model and the outcomes are graphed for visualisation. The validation of the findings from the qualitative analysis is shown in Figures (3.2a) and (3.2b) where the behaviours of the different sub-populations are illustrated. It can be seen from Figure (3.2a) that the system is stable for $R_0<1$ and Figure (3.2b) shows that the system is unstable for $R_0>1$. This validates the quantitative analysis and the numerical approach can therefore be used to find the solution as we vary the values of the parameters.



(a) All sub-populations when $R_0<1$



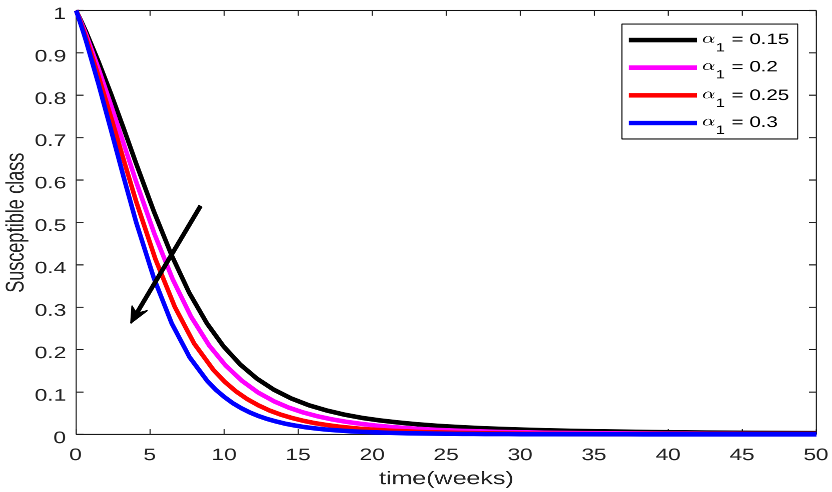
(b) All sub-populations when $R_0 > 1$

Figure 3.2: Verifying the stability of the equilibrium points

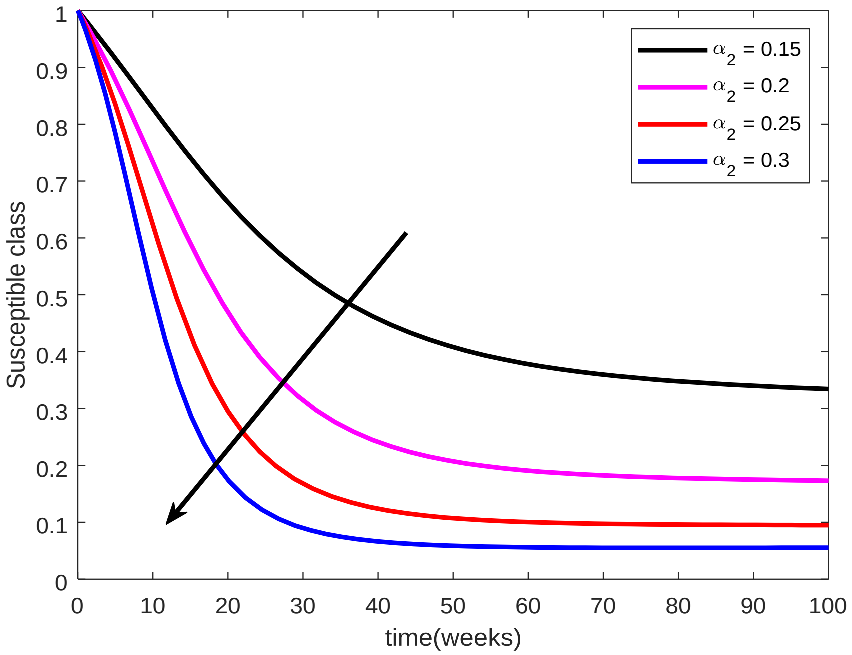
4.2 Discussion of Results

This study investigates COVID-19/tuberculosis co-infection in a population. The pertinent parameters are varied and the impact on the dynamics of both diseases is studied.

The rate at which the susceptible sub-population gets infected with COVID-19 is denoted as α_1 and the rate at which susceptible sub-population gets infected with tuberculosis is denoted as α_2. The rates are varied to investigate their effects on the five sub-populations and the outcomes are shown in Figures (4.1 – 4.5). As shown in Figure (4.1), increasing the rate at which individuals get infected with one disease will lead to the extinction of the susceptible sub-population. The consequence of increasing α_1 and α_2 is a rapid removal from the susceptible class and thus, a reduction in the susceptible class is expected. However, comparing Figures (4.1a) and (4.1b) shows that the effect of increasing rate of contracting tuberculosis is more significant than the influence of increasing rate of contracting COVID-19. Figure (4.2) illustrates the dynamics of the COVID-19 sub-population as the rate of contracting only COVID-19 and the rate of contracting only tuberculosis are varied. The COVID-19 sub-population continues to rise as the rate of contracting only COVID-19 increases while the COVID-19 sub-population reduces as the rate of contracting only tuberculosis increases. By comparing Figures (4.2a) and (4.2b), it can be seen that rates of increase in COVID-19 sub-population as α_1 increases are higher than the rate at which COVID-19 sub-population decreases with increasing α_2. Figure (4.3) shows that as the rate of single infection increases, the tuberculosis sub-population experiences an initial increase before the trend changes downward until there is no tuberculosis subpopulation any more. Figure (4.3a) depicts the response of the tuberculosis sub-population to an increase in the rate (α_1) of contracting COVID-19 only. The maximum population of the tuberculosis sub-population is obtained at the lowest α_1 and the peak of the COVID-19 subpopulation reduces with increasing α_1. Meanwhile, Figure (4.3b) shows that the response of the tuberculosis sub-population to an increase in the rate (α_2) of contracting tuberculosis only. The maximum population of the tuberculosis sub-population is obtained at the highest α_2 and the peak of the tuberculosis sub-population increases with increasing α_1. As the rate at which susceptible sub-populations get infected with only one disease increases, the co-infected sub-population increases. The increase is more pronounced when the rate of infection with tuberculosis only increases. Figures (4.4a) and (4.4b) show that the co-infected population increases with increasing rate of recruitment into any diseased sub-population. The recovered sub-population is shown in figure (4.5a) to reduce as the rate of getting COVID-19 only increases and figure (4.5b) shows that the recovered sub-population increases when the rate of getting tuberculosis only increases.

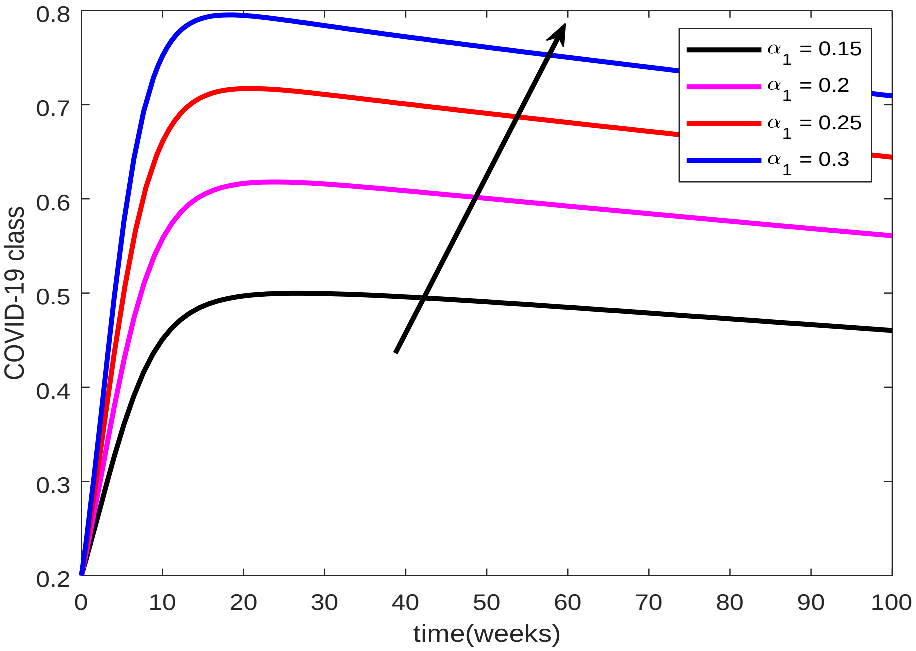


(a) Susceptible class with α_1

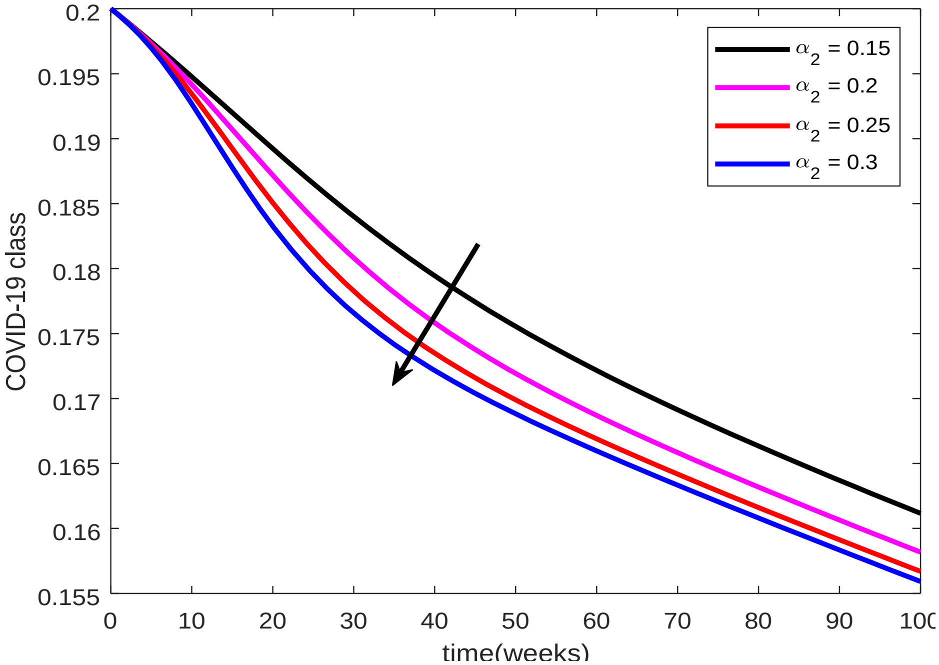


(b) Susceptible class with α_2

Figure 4.3: Susceptible class with rates of single infection

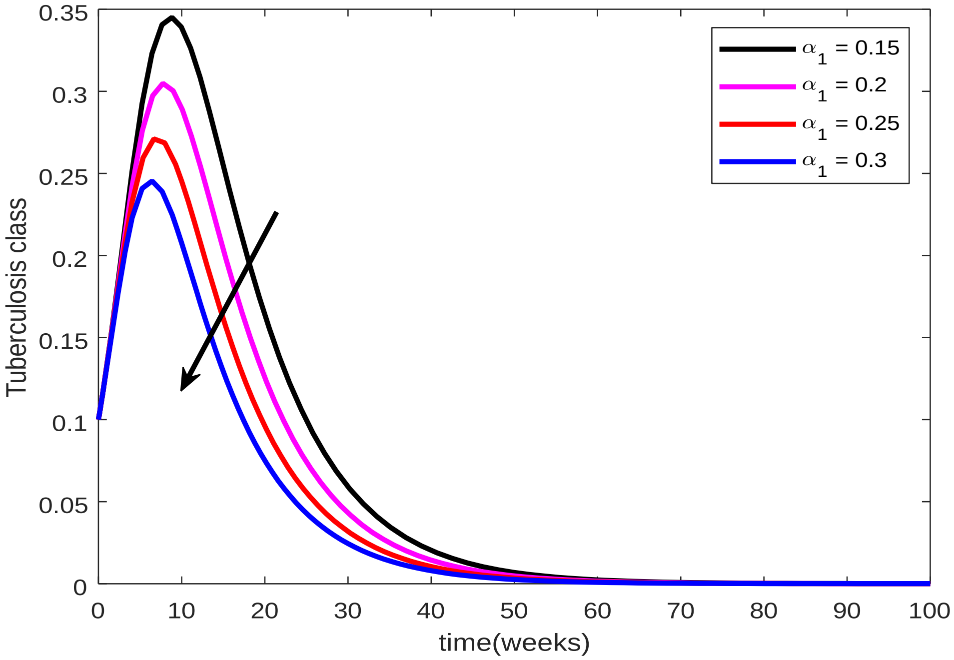


(a) COVID-19 class with α_1

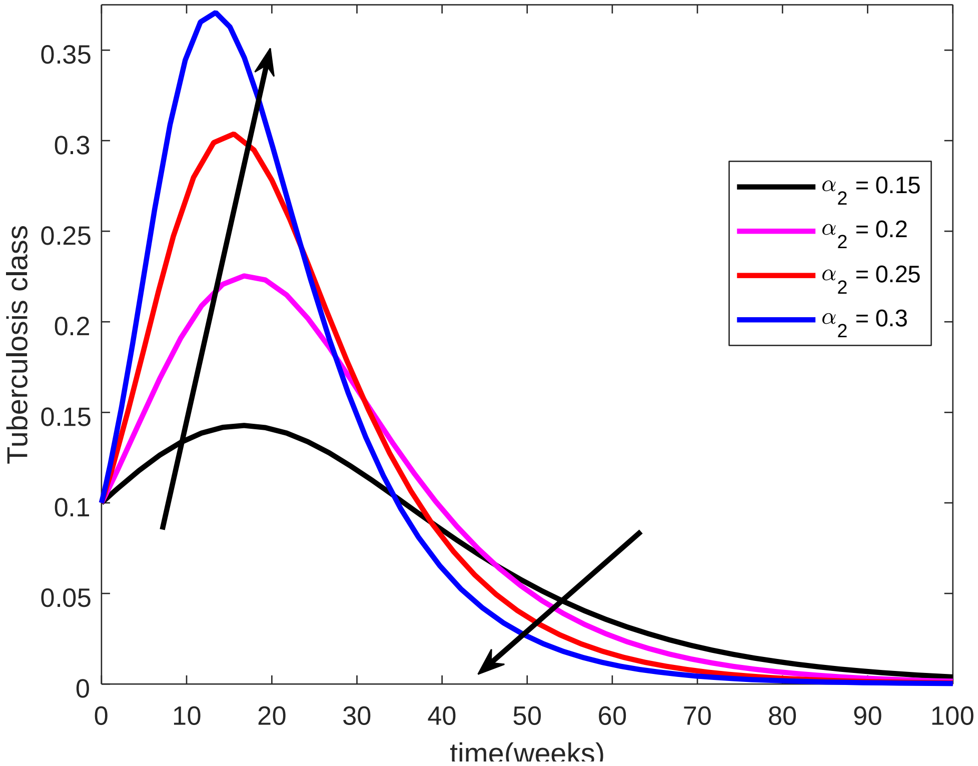


(b) COVID-19 class with α_2

Figure 4.4: COVID-19 class with rates of single infection

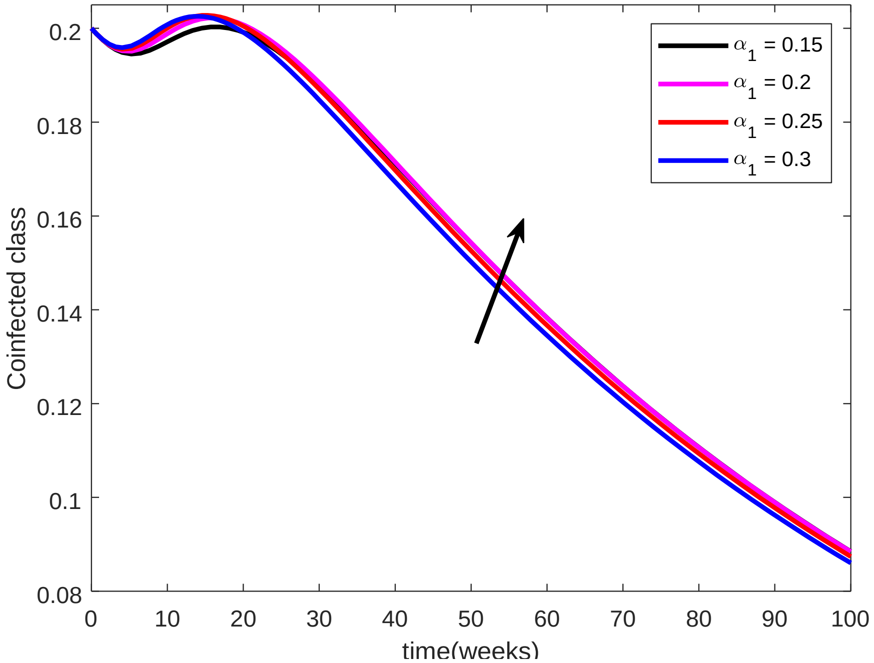


(a) Tuberculosis class with α_1

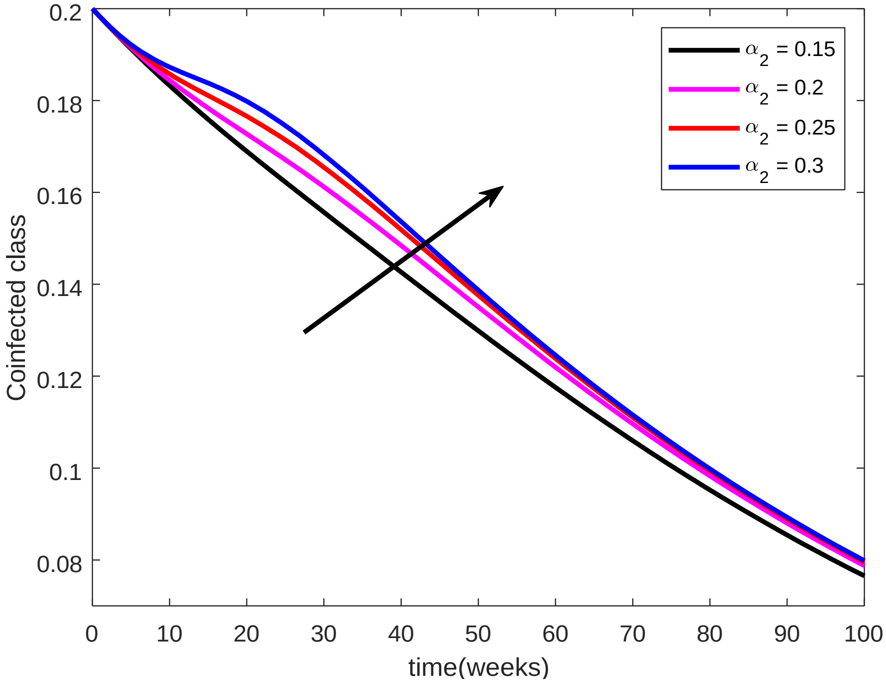


(b) Tuberculosis class with α_2

Figure 4.5: Tuberculosis class with rates of single infection

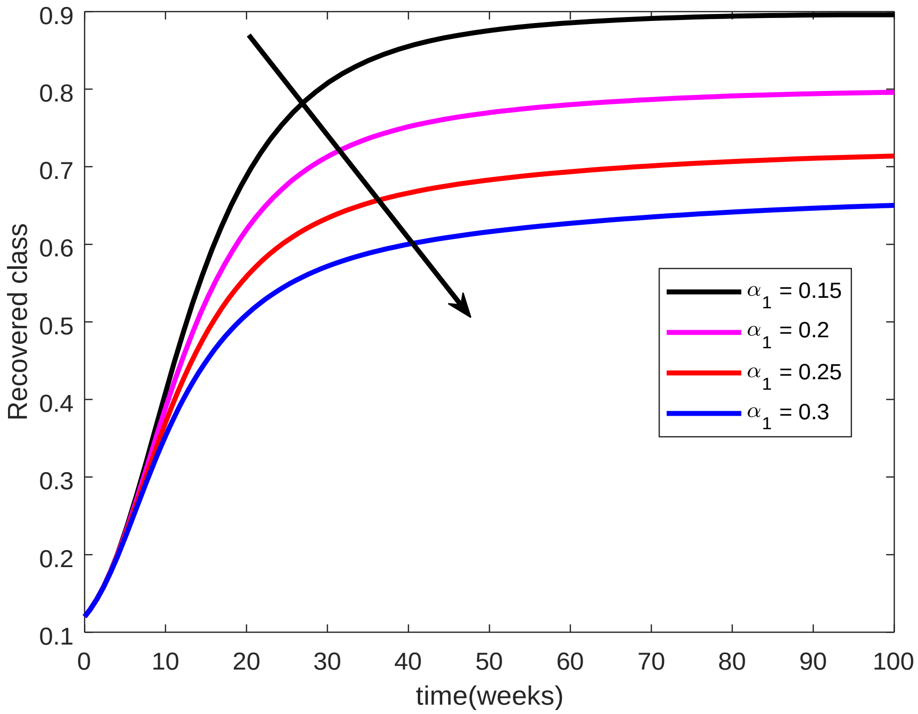


(a) Co-infected class with α_1

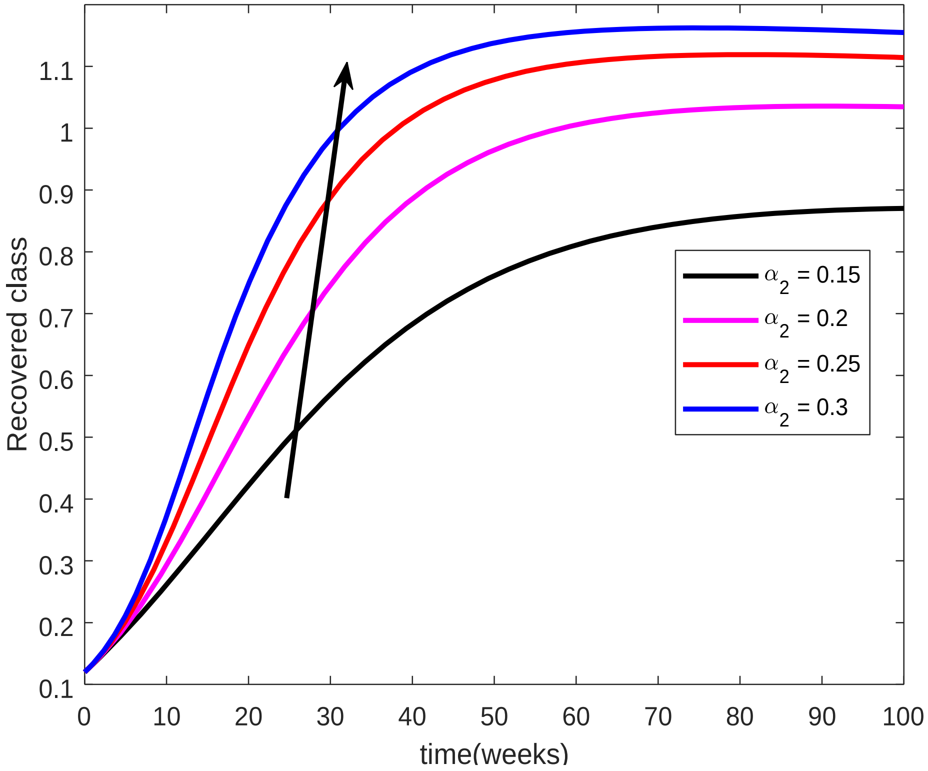


(b) Co-infected class with α_2

Figure 4.6: Co-infected class with rates of single infection



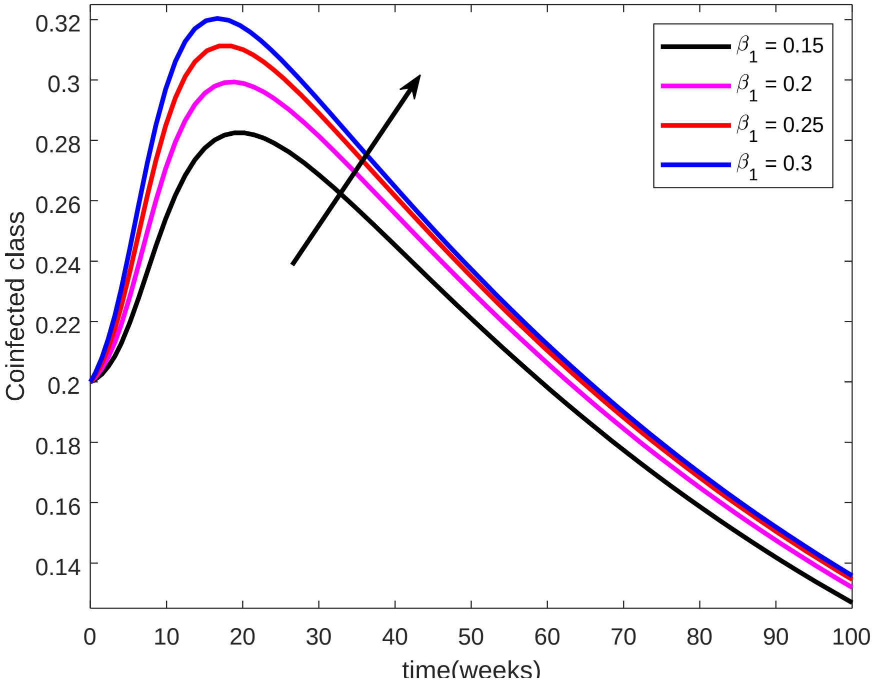
(a) Recovered class with α_1



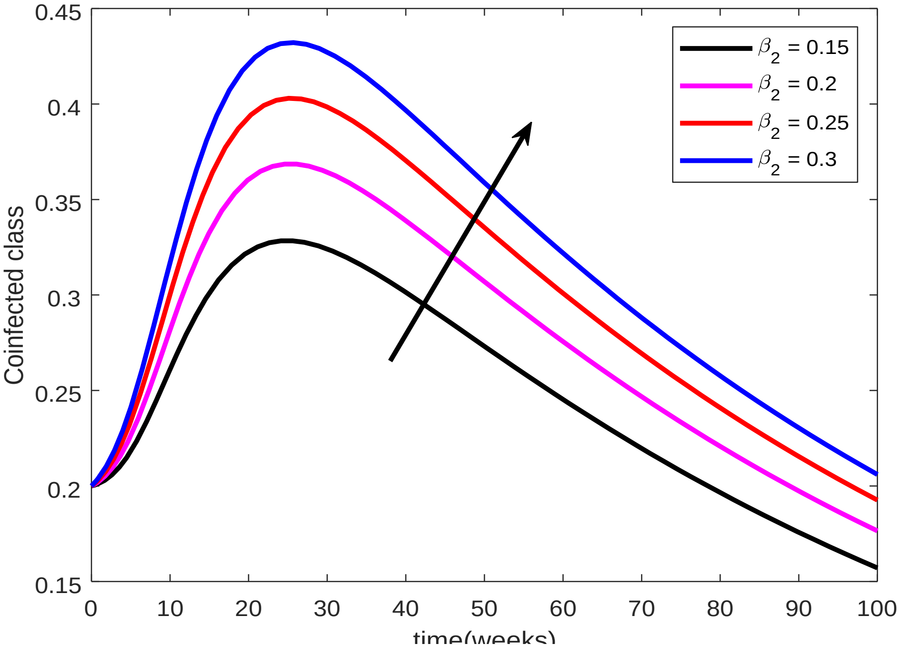
(b) Recovered class with α_2

Figure 4.7: Recovered class with rates of single infection

The next thing is to consider the response of co-infected and recovered sub-populations to the impact of migration rate β_1 from the COVID-19 sub-population to the co-infected subpopulation and migration rate β_2 from tuberculosis sub-population to co-infected subpopulation. As expected, migrations from COVID-19 to a co-infected sub-population or from tuberculosis to a co-infected sub-population will both result in the co-infected population increase. Figure (4.6) confirms the expectation and shows that the co-infected sub-population increases with increasing migration from a single disease compartment to the co-infected sub-population. Furthermore, the effects of migration from the tuberculosis sub-population are more significant than migration from COVID-19 (compare Figures (4.6a) and (4.6b)). Meanwhile, the recovered sub-population increases when migration from COVID-19 increases (as shown in Figure (4.7a)) but the recovered sub-population reduces if migration from tuberculosis to co-infected increases (see Figure (4.7b)).

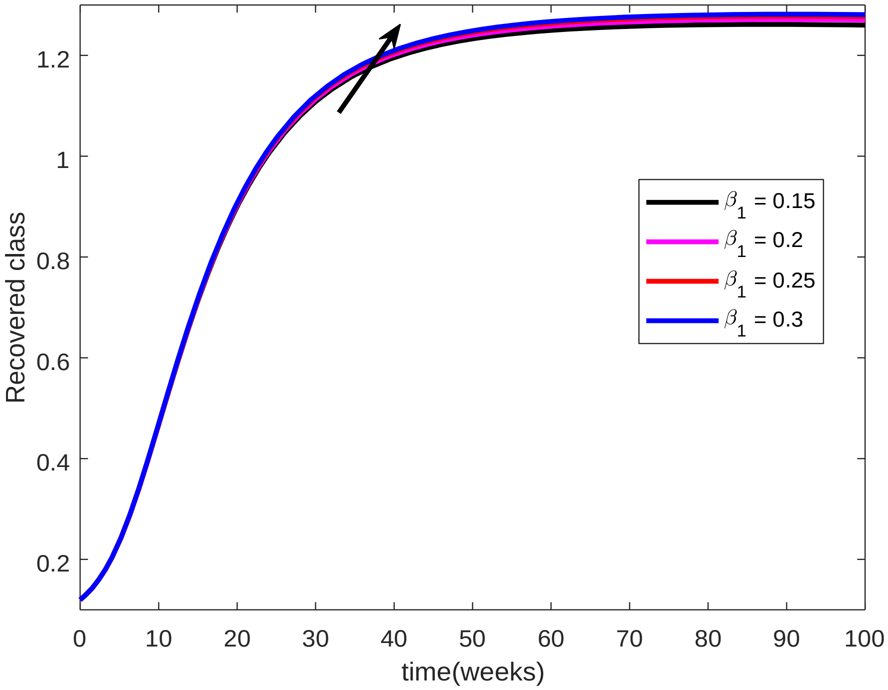


(a) Co-infected class with migration from COVID-19 to co-infected class

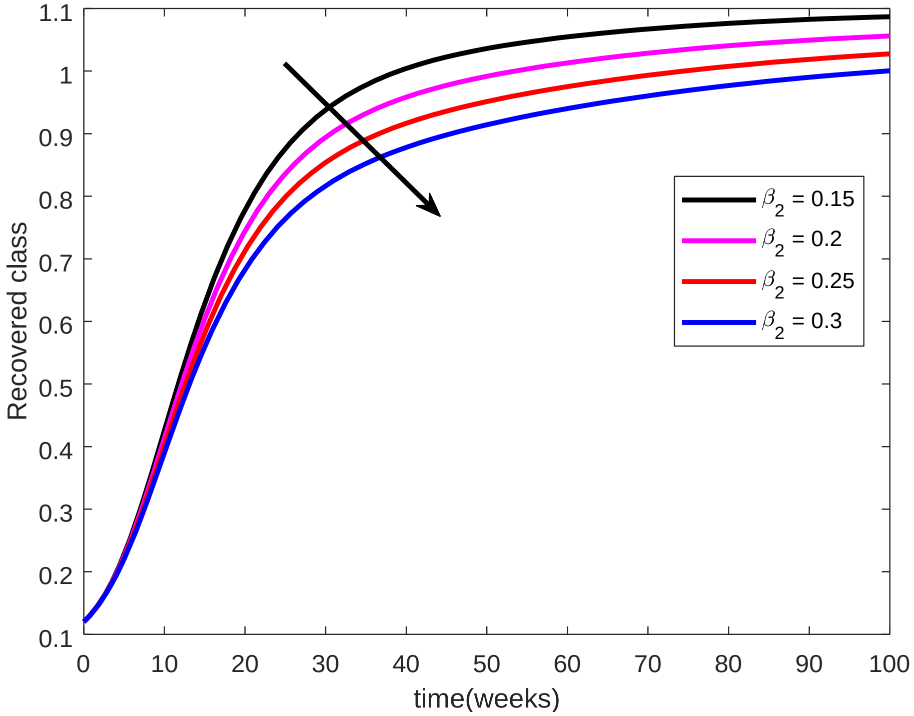


(b) Co-infected class with migration from tuberculosis to co-infected class

Figure 4.8: Co-infected class with migration to co-infected class from single infections



(a) Recovered class with migration from COVID-19 to co-infected compartment



(b) Recovered class with migration from tuberculosis to co-infected compartment

Figure 4.9: Recovered class with migration from single disease to co-infected compartment

5

CONCLUSION AND RECOMMENDATION

5.1 CONCLUSION

Investigation of the co-infection with COVID-19 and tuberculosis is carried out in this study. A deterministic model is formulated to explain the trend in COVID-19/tuberculosis co-infection in a population. The equilibria for the governing equations were obtained as

$$E_0=\left(\frac{\Lambda}{\mu},0,0,0\right)\wedge\left(S^{¿},E^{¿},C^{¿},T^{¿},I^{¿},R^{¿}\right)$$

where

$$S^{¿}=\frac{\Lambda}{\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}},R^{¿}=\frac{r_1}{\mu}C^{¿}+\frac{r_2}{\mu}T^{¿}+\frac{r_3}{\mu}I^{¿},$$

$$I^{¿}=\frac{\left(\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)\Lambda-\left(\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)\left(\left(\mu+d_1+r_1\right)C^{¿}-\left(\mu+d_2+r_2\right)T^{¿}\right)}{\left(\mu+d_1+d_2+r_3\right)\left(\mu+\alpha_1 C^{¿}+\alpha_2 T^{¿}\right)}.$$

The reproduction number is also calculated to track the number of possible new infections and we obtain the reproduction number as

$$R_0=max\left\{\frac{\alpha_1\Lambda}{\mu\left(\mu+d_1+r_1\right)},\frac{\alpha_2\Lambda}{\mu\left(\mu+d_2+r_2\right)},0\right\}.$$

The DFE point is established as locally asymptotically stable if $R_0<1$. The non-negativity condition for the model was established and the Runge-Kutta method of order 4 was used to solve the model. The model is simulated for various parameter values and the following outcomes are observed;

Increasing the rate at which individuals get infection with a single disease (either COVID-19 or tuberculosis) poses the risk of co-infecting every member of the population. Also, it is found that the rate of contracting tuberculosis poses more significant impact on the possibility of co-infection than COVID-19.

I. The maximum tuberculosis sub-population is obtained at the lowest rate of recruitment into the COVID-19 sub-population while the maximum COVID-19 sub-population is obtained at the highest rate of recruitment into the COVID-19 sub-population.

II.Migrations from COVID-19 to co-infected sub-population or from tuberculosis to co-infected sub-population both lead to the co-infected population increase. The effects of migration from tuberculosis sub-population is more significant than migration from COVID-19.

5.2 RECOMMENDATIONS

Premising on the results obtained from this project, the following recommendations are given;

i Since the rate of contracting tuberculosis poses more significant impact on the possibility of co-infection than COVID-19, caution has to be placed to ensure that COVID-19 is not allowed to thrive in the population where tuberculosis is rampant.

ii Stringent measures (such as the use of nose mask, travel restrictions, hand washing, periodic sanitizers, and social distancing) are necessary to prevent the tuberculosis from reaching the maximum. These measures are able to reduce recruitment into the COVID-19 sub-population.

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APPENDIX

MATLAB CODE

```
clc;
clear all;
format compact
global Lambda mu alpha_1 alpha_2 beta_1 beta_2 d_1 d_2 r_1 r_2 r_3
Lambda = 1000; mu = 0.06; alpha_1 = 0.1; alpha_2 = 0.1; beta_1 = 0.3;
beta_2 = 0.02; d_1=0.05; d_2=0.04; r_1=0.09; r_2 = 0.05; r_3 = 0.04;
i=0;

for beta_2 = [0.2,0.45,0.7]
   i=i+1; tspan=0:0.001:50; xzero=[300,10,10,10,10];
   [t,x]=ode45(@Equations,tspan,xzero); line_style = ["k-","r--","b-"];

   if i ~= 3
      figure(1),plot(t,x(:,1),line_style(i));
      figure(2),plot(t,x(:,2),line_style(i));
      figure(3),plot(t,x(:,3),line_style(i));
      figure(4),plot(t,x(:,4),line_style(i));
      figure(5),plot(t,x(:,5),line_style(i)); hold on
   else
      parameter_val = 'beta_1';
      txt = strcat("S_",parameter_val);
      figure(1),plot(t,x(:,1),line_style(i))
      xlabel('time (t)'), ylabel('Susceptible, S')
      saveas(gcf,txt)

      txt = strcat("C_",parameter_val);
      figure(2),plot(t,x(:,2),line_style(i))
      xlabel('time (t)'), ylabel('COVID-19 class, C')
      saveas(gcf,txt)

      txt = strcat("T_",parameter_val);
      figure(3),plot(t,x(:,3),line_style(i))
      xlabel('time (t)'),ylabel('Tuberculosis class, T')
      saveas(gcf,txt)

      txt = strcat("I_",parameter_val);
      figure(4),plot(t,x(:,4),line_style(i))
      xlabel('time (t)'),ylabel('Coinfected class, I')
      saveas(gcf,txt)

      txt = strcat("R_",parameter_val);
      figure(5),plot(t,x(:,5),line_style(i))
      xlabel('time (t)'),ylabel('Recovered class, R')
      saveas(gcf,'R_mu')
   end
end
function res=Equations(t,X)
   global Lambda mu alpha_1 alpha_2 beta_1 beta_2 d_1 d_2 r_1 r_2 r_3
   S = X(1); C = X(2); T = X(3); I = X(4); R = X(5);
   dx1 = Lambda - mu*S - alpha_1*S*C - alpha_2*S*T;
   dx2 = alpha_1*S*C - beta_1*C*T - (mu + d_1)*C - r_1*C;
   dx3 = alpha_2*S*T - beta_2*C*T - (mu + d_2)*T - r_2*T;
   dx4 = beta_1*C*T + beta_2*C*T - (mu + d_1 + d_2)*I - r_3*I;
   dx5 = r_1*C + r_2*T +r_3*I - mu*R;
   res = [dx1; dx2; dx3; dx4; dx5];
```

```
end
```