

Hopf bifurcation analysis of a TB infection model with two discrete time delays

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Abstract *This study proposes a nonlinear mathematical model to analyze tuberculosis (TB) infection dynamics, incorporating two-time delays. The model's fundamental properties are first examined, focusing on the stability of the disease-free and TB-endemic equilibria. The local stability analysis reveals that the disease-free equilibrium remains stable when the basic reproduction number $\mathcal{R}_0 < 1$, while the endemic equilibrium becomes stable when $\mathcal{R}_0 > 1$. Notably, the two-time delays induce Hopf bifurcation under specific conditions, leading to periodic solutions and oscillations in the system. These findings highlight the significant impact of time delays on the system's stability, with potential implications for understanding TB transmission dynamics. Numerical simulations are conducted to validate the theoretical predictions, demonstrating how variations in delay parameters can influence the system's behavior and stability, providing important insights for controlling TB outbreaks.*

1 Introduction

Tuberculosis (TB) is a widespread infectious disease that affects both humans and animals, caused by bacteria from the *Mycobacterium tuberculosis* complex, primarily *M. tuberculosis* and related species, with *M. tuberculosis* being known as Koch's bacillus. Although tuberculosis predominantly affects the lungs, it can occasionally target other organs and systems in the body. *Mycobacterium tuberculosis* is transmitted through airborne droplets when an infected person speaks, coughs, or sneezes. In most cases, the bacterium leads to latent infection, where the disease is inactive and asymptomatic. However, approximately one in ten latent infections eventually progress to active tuberculosis. According to 2021 data, TB remains the leading cause of death from a single infectious agent, affecting approximately 10 million people annually and resulting in about 1.5 million deaths globally [1].

Despite being treatable and preventable, the widespread prevalence of tuberculosis underscores the need for a deeper understanding of its transmission dynamics. Mathematical modeling plays a fundamental role in this process, serving as a crucial tool for analyzing and controlling the spread of the disease. Techniques such as ordinary differential equations (ODEs), partial differential equations (PDEs), and time-delay equations are commonly employed to predict infection dynamics and design effective control strategies for diseases like tuberculosis.

Extensive mathematical work has been conducted using ODEs in epidemiology, particularly in modeling infectious diseases such as tuberculosis. ODEs are essential for understanding disease transmission dynamics, as they provide a framework to describe transitions between different population states, such as susceptible, infected, recovered, and re-susceptible (SIRS). One of the foundational models for tuberculosis transmission was proposed by Waaler and Anderson in 1962, marking a significant advancement in the study of TB dynamics [2]. Later, Yang et

al. expanded upon these models, contributing further to the mathematical framework for understanding the transmission of tuberculosis [3]. Ullah et al. focused on TB models incorporating incomplete treatment, providing critical insights into how treatment gaps affect disease progression [4]. Dany Moualeu-Ngangue et al. analyzed a tuberculosis model with multiple latent classes, offering a deeper understanding of TB dynamics in populations with various stages of latent infection [5]. Other researchers, such as Das and the other authors, also refined tuberculosis models, improving our ability to predict transmission patterns and influence public health strategies [6]. ODE-based models have proven crucial for predicting the spread of tuberculosis and designing effective control measures [7, 8].

In addition to these foundational studies, substantial research has focused on the use of linear systems in tuberculosis modeling. Researchers like Carlos Castillo-Chavez [9, 10] have incorporated nonlinear incidence and treatment functions into TB transmission models, adding realism to the models. While these models explain disease spread effectively, they fall short in accounting for the historical progression of tuberculosis. As such, the inclusion of delay differential equations (DDEs) is essential for a more accurate representation of disease dynamics, as delays account for the temporal aspects of disease progression and intervention effects. The introduction of delays, including fractional delays, has been explored by researchers such as Mohammed A. Almalahi et al. [11], highlighting the importance of these delays in improving the predictive accuracy of models [12] also see [13].

The paper's novelty lies in incorporating two time delays into the tuberculosis transmission model. This adds realism by acknowledging the time lag between the onset of symptoms and treatment. The study's bifurcation analysis offers valuable insights into the dynamic behavior of the disease under different conditions, which is a significant contribution to the field.

Building on the work mentioned above, we propose a mathematical model for tuberculosis infection that incorporates two time delays, τ_1 and τ_2 . The novelty of this study lies in examining the dynamics of tuberculosis transmission with these two delays, which enhances our understanding of the disease's progression. Our goal is to analyze how these delays affect the stability and behavior of the system, ultimately informing better strategies for controlling TB spread. To investigate the model's qualitative behavior, we apply stability theory for nonlinear differential equations [14, 15], which helps us understand the impact of incorporating time delays on the system's stability and tuberculosis transmission dynamics. This research underscores the importance of mathematical epidemiology in managing and understanding tuberculosis.

The structure of this paper is as follows: Section 2 presents a nonlinear mathematical model that includes two delays, along with a discussion on the existence of its solutions. Section 3 focuses on determining the equilibrium points. Section 4 investigates the local stability of the equilibrium points and provides a detailed analysis of Hopf bifurcation, identifying conditions under which periodic solutions may arise. Section 5 presents numerical simulations to support the analytical results and to illustrate the emergence of oscillatory behavior in the system.

2 Model formulation

To analyze the kinetics of TB infection transmission, we present a three-dimensional deterministic nonlinear mathematical model utilizing delay differential equations. In order to create the model, the total population $N(t)$ is divided into three sub-populations: the susceptible population $S(t)$, the Tuberculosis-infected individuals $I(t)$, and the recovered individuals $R(t)$, such that $N(t) = S(t) + I(t) + R(t)$. TB infection spreads more gradually than many other diseases, so the incidence rate must be used in the analysis. The force of infection for TB is expressed by the formula $\frac{\beta_1 I(t) S(t)}{1 + \alpha I(t)}$, where β_1 represents the contact rate with infected individuals, and α is a parameter that measures the inhibitory effect on transmission, reflecting the saturation effect.

When individuals do not receive prompt TB infection detection, a time delay occurs. To account for this delay, we introduce the parameter τ_1 , which represents the time between infection and the onset of symptoms. This delay reflects the incubation period during which infected individuals may unknowingly transmit the disease. Consequently, the force of infection is adjusted to:

$$\frac{\beta_1 I(t - \tau_1) S(t - \tau_1)}{1 + \alpha I(t - \tau_1)}.$$

This model illustrates that although the number of infected individuals may increase, the infection rate does not grow indefinitely due to behavioral changes and other factors affecting the spread of the disease.

Individuals transition from the population infected with the tuberculosis virus to the recovered population at a rate of β_2 , with a delay τ_2 in receiving immediate treatment. The parameter τ_2 reflects the time between symptom onset and the initiation of treatment, accounting for delays in diagnosis and treatment initiation. This transition is represented as $\beta_2 I(t - \tau_2)$. Subsequently, they move to the susceptible population $S(t)$ at a rate of σ after recovering from tuberculosis. Finally, Π is the recruitment rate, μ is the natural death rate, and μ_I is the TB-induced death rate.

The mathematical model can be constructed using the information provided, along with the assumptions. The delay differential equations are expressed in the following form:

$$\begin{cases} \frac{dS(t)}{dt} = \Pi - \frac{\beta_1 S(t - \tau_1) I(t - \tau_1)}{1 + \alpha I(t - \tau_1)} - \mu S(t) + \sigma R(t), \\ \frac{dI(t)}{dt} = \frac{\beta_1 S(t - \tau_1) I(t - \tau_1)}{1 + \alpha I(t - \tau_1)} - (\mu + \mu_I + \beta_2) I(t), \\ \frac{dR(t)}{dt} = \beta_2 I(t - \tau_2) - (\mu + \sigma) R(t), \end{cases} \tag{2.1}$$

the initial conditions for system (2.1) take the form

$$S(\varphi) = \psi_1(\varphi) > 0, I(\varphi) = \psi_2(\varphi) > 0, R(\varphi) = \psi_3(\varphi) > 0 \text{ on } \varphi \in [-\tilde{\tau}, 0], \tag{2.2}$$

where $\tilde{\tau} = \max\{\tau_1, \tau_2\}$ and $(\psi_1, \psi_2, \psi_3)^T \in C(\max[-\tilde{\tau}, 0], \mathbb{R}^3)$ as a Banach space of continuous function from $[-\tilde{\tau}, 0]$ into \mathbb{R}^3 .

2.1 Non-negativity and boundedness of solutions

In this section, we delve into the investigation of the existence, non-negativity and boundedness of solutions within the context of system (2.1)-(2.2). Our primary objective at the outset is to determine whether a viable solution exists for this particular system. To facilitate our analysis, we express system (2.1)-(2.2) in the following form

$$\frac{dX}{dt} = AX(t) + F(X_\tau(t)) = G(X(t), X_\tau(t)), \tag{2.3}$$

where

$$X(t) = \begin{pmatrix} S(t) \\ I(t) \\ R(t) \end{pmatrix}, X_\tau(t) = X(t - \tau),$$

$$A = \begin{pmatrix} -\mu & 0 & \sigma \\ 0 & -(\mu + \mu_I + \beta_2) & 0 \\ 0 & 0 & -(\mu + \sigma) \end{pmatrix}, F(X_\tau(t)) = \begin{pmatrix} \Pi - \frac{\beta_1 I(t-\tau_1)}{1+\alpha I(t-\tau_1)} S(t - \tau_1) \\ \frac{\beta_1 I(t-\tau_1)}{1+\alpha I(t-\tau_1)} S(t - \tau_1) \\ \beta_2 I(t - \tau_2) \end{pmatrix}.$$

and there exists $L > 0$ such that

$$|F(X_{1\tau}(t)) - F(X_{2\tau}(t))| \leq L|X_{1\tau}(t) - X_{2\tau}(t)|,$$

with

$$|X_{1\tau}(t) - X_{2\tau}(t)| = |S_{1\tau}(t) - S_{2\tau}(t)| + |I_{1\tau}(t) - I_{2\tau}(t)| + |R_{1\tau}(t) - R_{2\tau}(t)|,$$

Moreover, we get

$$|G(X_1(t), X_{1\tau}(t)) - G(X_2(t), X_{2\tau}(t))| \leq K(|X_1(t) - X_2(t)| + |X_{1\tau}(t) - X_{2\tau}(t)|),$$

where $K = \max\{\|A\|, L\} < +\infty$. Thus, it follows that the function G is uniformly Lipschitz continuous. Then the system (2.1)-(2.2) has unique solution.

To ensure the positivity and boundedness of the solution and from a biological perspective, we examine system (2.1)-(2.2) within the practical domain

$$\Omega = \left\{ (S, I, R) \in \mathbb{R}_+^3 : S + I + R \leq \frac{\Pi}{\mu} \right\}. \quad (2.4)$$

To establish the non-negativity and boundedness of solutions, we can apply the approach presented in the article [16], where it is shown that the system solutions remain non-negative and bounded within the practical domain defined by equation (2.4). This ensures that all solutions of our model stay biologically feasible (i.e., non-negative and bounded) for all $\tau_1, \tau_2 > 0$.

3 Existence of equilibrium points

In this section, we determine the conditions under which the equilibrium point of the system (2.1)-(2.2) exists in the absence of two delay times, τ_1 and τ_2 . The mathematical model has two equilibrium points, the first is the disease-free equilibrium E^0 which exists in the absence of any disease and other the corresponds to TB infection state E^* .

In the absence of TB infection ($I \equiv 0$), the disease-free equilibrium E^0 of system (2.1)-(2.2) provided by

$$E^0 = (S^0, I^0, R^0) = \left(\frac{\Pi}{\mu}, 0, 0 \right). \quad (3.1)$$

In epidemiology, the basic reproduction number of the disease, denoted \mathcal{R}_0 , is the number of secondary infections resulting from a single primary infection in an otherwise susceptible population. Mathematically, \mathcal{R}_0 is looked on as a threshold, depending on epidemiological parameters of the model, that ensures or not the stability of an equilibrium point called disease-free equilibrium when the latter exists. By using the next-generation matrix approach [17, Chapter 9], the basic reproduction number \mathcal{R}_0 of system (2.1)-(2.2), is given by

$$\mathcal{R}_0 = \frac{\beta_1 \Pi}{\mu(\mu + \mu_I + \beta_2)}. \quad (3.2)$$

Remark 3.1. The parameters α and σ do not appear in the expression of the basic reproduction number \mathcal{R}_0 , as it quantifies new infections generated by a single infected individual in a fully susceptible population. However, the saturation rate α and the rate σ , which represents the return of recovered individuals to the susceptible class due to loss of immunity following recovery from tuberculosis, influence the epidemic dynamics at later stages.

Next, we consider the case where TB infection is present. Let $E^* = (S^*, I^*, R^*)$ be an equilibrium point of system (2.1)-(2.2). Then, it must satisfy

$$\begin{cases} \Pi - \frac{\beta_1 I^* S^*}{1 + \alpha I^*} - \mu S^* + \sigma R^* = 0, \\ \frac{\beta_1 I^* S^*}{1 + \alpha I^*} - (\mu + \mu_I + \beta_2) I^* = 0, \\ \beta_2 I^* - (\mu + \sigma) R^* = 0. \end{cases} \quad (3.3)$$

Then,

$$\begin{aligned} S^* &= \frac{\delta}{\alpha\mu^3 + (\alpha(\beta_2 + \mu_I + \sigma) + \beta_1)\mu^2 + \beta_1\sigma\mu_I + ((\beta_1 + \alpha\sigma)(\beta_2 + \mu_I) + \beta_1\sigma)\mu}, \\ I^* &= \frac{\mu(\sigma + \mu)(\mu + \mu_I + \beta_2)(\mathcal{R}_0 - 1)}{\alpha\mu^3 + (\alpha(\beta_2 + \mu_I + \sigma) + \beta_1)\mu^2 + \beta_1\sigma\mu_I + ((\beta_1 + \alpha\sigma)(\beta_2 + \mu_I) + \beta_1\sigma)\mu}, \\ R^* &= \frac{\mu(\mu + \mu_I + \beta_2)\beta_2(\mathcal{R}_0 - 1)}{\alpha\mu^3 + (\alpha(\beta_2 + \mu_I + \sigma) + \beta_1)\mu^2 + \beta_1\sigma\mu_I + ((\beta_1 + \alpha\sigma)(\beta_2 + \mu_I) + \beta_1\sigma)\mu}, \end{aligned} \quad (3.4)$$

where $\delta > 0$, and is given by

$$\delta = (\Pi\alpha + 2\beta_2 + \sigma + 2\mu_I)\mu^2 + \mu^3 + (\Pi\alpha(\beta_2 + \mu_I) + \beta_2\mu_I + \mu_1^2)\sigma + (\Pi\alpha(\beta_2 + \mu_I) + \beta_2^2 + (\Pi\alpha + \beta_2 + 2\mu_I)\sigma + 2\beta_2\mu_I + \mu_1^2 + \beta_2^2)\mu.$$

We now present the following result regarding the existence of equilibrium points of system (2.1)-(2.2)

Theorem 3.2. For system (2.1)-(2.2) there always exists a disease-free equilibrium point $E^0 = (\frac{\Pi}{\mu}, 0, 0)$; and if $\mathcal{R}_0 > 1$, then there also exists an endemic equilibrium point $E^* = (S^*, I^*, R^*)$.

4 Local stability and Hopf bifurcations

In this section, our primary focus is to thoroughly examine the dynamics of the solution trajectories in the vicinity of two key equilibrium points: the disease-free equilibrium point E^0 and the endemic equilibrium point E^* , as defined in (3.4). To accomplish this, we will delve into the local stability and Hopf bifurcation of these equilibrium points. This analysis will be conducted by studying the characteristic equation of the linearized system around its equilibrium points.

4.1 Local stability of the disease-free equilibrium E^0

Within this section, we investigate the local stability of the disease-free equilibrium point E^0 of system (2.1)-(2.2). To do so, we begin by introducing the following perturbation variables

$$\bar{S}(t) = S(t) - S^0, \bar{I}(t) = I(t), \bar{R}(t) = R(t).$$

Next, we can express the linearized system of system (2.1)-(2.2) around the disease-free equilibrium point E^0 in the following manner

$$\begin{cases} \frac{d\bar{S}(t)}{dt} = -\mu\bar{S}(t) - \beta_1 \frac{\Pi}{\mu} \bar{I}(t - \tau_1) + \sigma\bar{R}(t), \\ \frac{d\bar{I}(t)}{dt} = \beta_1 \frac{\Pi}{\mu} \bar{I}(t - \tau_1) - (\mu + \mu_I + \beta_2)\bar{I}(t), \\ \frac{d\bar{R}(t)}{dt} = \beta_2 \bar{I}(t - \tau_2) - (\mu + \sigma)\bar{R}(t). \end{cases} \tag{4.1}$$

Furthermore, by considering the exponential solutions $\bar{S}(t) = x_1 e^{\lambda t}, \bar{I}(t) = x_2 e^{\lambda t}, \bar{R}(t) = x_3 e^{\lambda t}$, we substitute them into the linear system (4.1). This allows us to write the characteristic equation at the disease-free equilibrium E^0 , as follows

$$\begin{vmatrix} \lambda + \mu & \beta_1 \frac{\Pi}{\mu} e^{-\lambda\tau_1} & -\sigma \\ 0 & \lambda + \mu + \mu_I + \beta_2 - \beta_1 \frac{\Pi}{\mu} e^{-\lambda\tau_1} & 0 \\ 0 & -\beta_2 e^{-\lambda\tau_2} & (\lambda + \mu + \sigma) \end{vmatrix} = 0. \tag{4.2}$$

Thus

$$(\lambda + \mu)(\lambda + \sigma + \mu)(\lambda + \mu + \mu_I + \beta_2 - \beta_1 \frac{\Pi}{\mu} e^{-\lambda\tau_1}) = 0. \tag{4.3}$$

Here, we will consider two cases. If $\tau_1 = 0$, then equation (4.3) becomes as follows

$$(\lambda + \mu)(\lambda + \sigma + \mu)(\lambda + \mu + \mu_I + \beta_2 - \beta_1 \frac{\Pi}{\mu}) = 0. \tag{4.4}$$

Note that, equation (4.4) has three different roots which are given by $\lambda_1 = -\mu, \lambda_2 = -(\sigma + \mu)$ and $\lambda_3 = -(\mu + \mu_I + \beta_2) + \beta_1 \frac{\Pi}{\mu}$. It is evident to observe that all roots $\lambda_j, j = 1, 2, 3$ have negative real parts, if $\mathcal{R}_0 < 1$, while the third root λ_3 is a positive root wherever $\mathcal{R}_0 > 1$. Therefore, the disease-free equilibrium point is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$ for $\tau_1 = 0$.

Next, we jump to treat the case when $\tau_1 > 0$. In this case, the roots of equation (4.3) are given by $\lambda_1 = -\mu$, $\lambda_2 = -(\sigma + \mu)$ and the third one denoted by λ_3 is determined by the solution of the following equation

$$f(\lambda) = (\lambda + \mu + \mu_I + \beta_2 - \beta_1 \frac{\Pi}{\mu} e^{-\lambda\tau_1}) = 0. \quad (4.5)$$

Note that, for λ real, it is readily seen that $\lim_{\lambda \rightarrow \infty} f(\lambda) = +\infty$, and $f(0) = (\mu + \mu_I + \beta_2)(1 - \mathcal{R}_0) < 0$, if $\mathcal{R}_0 > 1$. Hence, with the help of Intermediate Value Theorem [18, Theorem 4.23, page 93], it follows that equation $f(\lambda) = 0$ has a positive real root if $\mathcal{R}_0 > 1$.

Now, if $\mathcal{R}_0 < 1$, we suppose that $\Re(\lambda) \geq 0$, then by taking the real part of equation (4.5), we get

$$\begin{aligned} \Re(\lambda) &= \beta_1 \frac{\Pi}{\mu} e^{-\Re(\lambda)\tau_1} \cos(\Im(\lambda)\tau_1) - (\mu + \mu_I + \beta_2) \\ &< (\mu + \mu_I + \beta_2)(\mathcal{R}_0 - 1) < 0, \end{aligned} \quad (4.6)$$

which is a contradiction with $\Re(\lambda) \geq 0$. Then, we can deduce that λ is a root of equation (4.5) with negative real part, if $\mathcal{R}_0 < 1$.

Remark 4.1. According to [19, Theorem 2, P.76], the local stability or instability of a linearized system leads to the local stability or instability of a nonlinear system.

Thus, the following theorem summarizes the above discussion.

Theorem 4.2. The disease-free equilibrium E^0 of system (2.1)-(2.2) is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Remark 4.3. In epidemiology, Theorem 4.2 implies that TB disease can be eliminated from the population whenever the basic reproduction number $\mathcal{R}_0 < 1$, if the initial sizes of the population of the model are in the basin of attraction of the disease-free equilibrium E^0 .

Remark 4.4. From above discussion, we can note that the local stability of the disease-free equilibrium does not depend on the time delays τ_1 and τ_2 .

4.2 Local stability of the endemic equilibrium point E^*

In this part, we follow a similar approach to [20], to study the local stability and Hopf-Bifurcation of the endemic equilibrium point E^* of system (2.1)-(2.2). To begin, we introduce the following perturbation variables

$$\tilde{S}(t) = S(t) - S^*, \quad \tilde{I}(t) = I(t) - I^*, \quad \tilde{R}(t) = R(t) - R^*,$$

where S^* , I^* and R^* are given in (3.4). Then, the linearized system around the endemic equilibrium $E^* = (S^*, I^*, R^*)$ can be expressed as follows

$$\begin{cases} \frac{d\tilde{S}(t)}{dt} = a_{11}\tilde{S}(t - \tau_1) + a_{12}\tilde{S}(t) + a_{13}\tilde{I}(t - \tau_1) + a_{14}\tilde{R}(t), \\ \frac{d\tilde{I}(t)}{dt} = a_{21}\tilde{S}(t - \tau_1) + a_{22}\tilde{I}(t - \tau_1) + a_{23}\tilde{I}(t), \\ \frac{d\tilde{R}(t)}{dt} = a_{31}\tilde{I}(t - \tau_2) + a_{32}\tilde{R}(t), \end{cases} \quad (4.7)$$

where

$$\begin{aligned} a_{11} &= -\frac{\beta_1 I^*}{(1 + \alpha I^*)}, & a_{12} &= -\mu, & a_{13} &= -\frac{\beta_1 S^*}{(1 + \alpha I^*)^2}, & a_{14} &= \sigma, & a_{21} &= \frac{\beta_1 I^*}{(1 + \alpha I^*)}, \\ a_{22} &= \frac{\beta_1 S^*}{(1 + \alpha I^*)^2}, & a_{23} &= -\left(\mu + \mu_I + \beta_2\right), & a_{31} &= \beta_2, & a_{32} &= -(\mu + \sigma). \end{aligned}$$

Further, setting $\tilde{S}(t) = y_1 e^{\lambda t}$, $\tilde{I}(t) = y_2 e^{\lambda t}$ and $\tilde{R}(t) = y_3 e^{\lambda t}$. By substituting these variables into system (4.7), it yields that the characteristic equation of linear system (4.7) can be written as follows

$$\begin{vmatrix} \lambda - a_{11}e^{-\lambda\tau_1} - a_{12} & -a_{13}e^{-\lambda\tau_1} & -a_{14} \\ -a_{21}e^{-\lambda\tau_1} & \lambda - a_{22}e^{-\lambda\tau_1} - a_{23} & 0 \\ 0 & -a_{31}e^{-\lambda\tau_2} & \lambda - a_{32} \end{vmatrix} = 0. \tag{4.8}$$

Thus, we could get

$$(\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0) + (m_1\lambda + m_0)e^{-2\lambda\tau_1} + (c_2\lambda^2 + c_1\lambda + c_0)e^{-\lambda\tau_1} + pe^{-\lambda(\tau_1+\tau_2)} = 0, \tag{4.9}$$

where

$$\begin{aligned} b_2 &= -a_{12} - a_{23} - a_{32}, & b_1 &= a_{12}a_{23} + a_{12}a_{32} + a_{23}a_{32}, \\ b_0 &= -a_{12}a_{23}a_{32}, & m_1 &= -a_{13}a_{21} + a_{11}a_{22}, \\ m_0 &= -a_{11}a_{22}a_{32} + a_{32}a_{13}a_{21}, & c_2 &= -a_{11} - a_{22}, \\ c_1 &= a_{11}a_{23} + a_{11}a_{32} + a_{12}a_{22} + a_{22}a_{32}, \\ c_0 &= -a_{11}a_{23}a_{32} - a_{12}a_{22}a_{32}, & p &= -a_{14}a_{21}a_{31}. \end{aligned}$$

Next, before going on, we multiply both ends of equation (4.9) by $e^{\lambda\tau_1}$, resulting in

$$(\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0)e^{\lambda\tau_1} + (m_1\lambda + m_0)e^{-\lambda\tau_1} + (c_2\lambda^2 + c_1\lambda + c_0) + pe^{-\lambda\tau_2} = 0. \tag{4.10}$$

At this stage, we will consider four different cases for the time delays τ_1 and τ_2 , as follows:

Case 1: $\tau_1 = \tau_2 = 0$. In this case, the characteristic equation (4.10) becomes

$$\lambda^3 + q_1\lambda^2 + q_2\lambda + q_3 = 0, \tag{4.11}$$

where

$$q_1 = c_2 + b_2, \quad q_2 = c_1 + b_1 + m_1, \quad q_3 = c_0 + b_0 + m_0 + p.$$

The Routh-Hurwitz Criterion [21], helps determine that equation (4.11) admits roots with negative real parts if the following condition, denoted as **C0**, is satisfied.

C0. $q_1 > 0$, $q_3 > 0$ and $q_1q_2 - q_3 > 0$.

In this case, we have the following conclusion regarding the local stability of the endemic equilibrium point E^* .

Theorem 4.5. The endemic equilibrium point E^* of system (2.1)-(2.2) is locally asymptotically stable if **C0** holds.

Remark 4.6. Theorem 4.5 indicates that TB disease will be able to start spreading through the population when condition **C0** holds, if the initial sizes of the model population are in the basin of attraction of the endemic equilibrium E^* .

Case 2: $\tau_1 = 0$ and $\tau_2 > 0$. Here, the characteristic equation (4.10) is given by

$$\lambda^3 + u_2\lambda^2 + u_1\lambda + u_0 + pe^{-\lambda\tau_2} = 0, \tag{4.12}$$

where

$$u_2 = c_2 + b_2, \quad u_1 = c_1 + b_1 + m_1, \quad u_0 = c_0 + b_0 + m_0.$$

Now, in order to investigate this case, we suppose that equation (4.12) has purely imaginary root of the form $\lambda = iw_2$, with $w_2 > 0$. Then, by substituting it into equation (4.12) and by taking its real and imaginary parts, we can find

$$\begin{cases} -u_2w_2^2 + u_0 + p \cos(w_2\tau_2) = 0, \\ -w_2^3 + u_1w_2 - p \sin(w_2\tau_2) = 0. \end{cases} \tag{4.13}$$

Next, by squaring and adding both equations of (4.13), we obtain

$$w_2^6 + (u_2^2 - 2u_1)w_2^4 + (u_1^2 - 2u_2u_0)w_2^2 + u_0^2 - p^2 = 0. \quad (4.14)$$

Later, setting $z = w_2^2$, then equation (4.14) can be rewritten as follows

$$\ell_1(z) = z^3 + (u_2^2 - 2u_1)z^2 + (u_1^2 - 2u_2u_0)z + u_0^2 - p^2 = 0. \quad (4.15)$$

Note that the derivative of the function $\ell_1(z)$ is given by

$$\ell_1'(z) = 3z^2 + 2(u_2^2 - 2u_1)z + (u_1^2 - 2u_2u_0).$$

To treat this case, let us set

$$\mathbf{C1.} \quad u_0^2 - p^2 \geq 0, \Delta_{\ell_1} = 4((u_2^2 - 2u_1)^2 - 3(u_1^2 - 2u_2u_0)) \leq 0;$$

$$\mathbf{C2.} \quad u_0^2 - p^2 \geq 0, \Delta_{\ell_1} > 0, z^* = \frac{-(u_2^2 - 2u_1) + \sqrt{(u_2^2 - 2u_1)^2 - 3(u_1^2 - 2u_2u_0)}}{3} < 0;$$

$$\mathbf{C3.} \quad u_0^2 - p^2 \geq 0, \Delta_{\ell_1} > 0, z^* > 0, \ell_1(z^*) > 0;$$

$$\mathbf{C4.} \quad u_0^2 - p^2 \geq 0, \Delta_{\ell_1} > 0, z^* > 0, \ell_1(z^*) < 0;$$

$$\mathbf{C5.} \quad u_0^2 - p^2 < 0.$$

With the help of Lemma .1 (see Appendix A.), if either condition C4 or condition C5 is satisfied, then the equation $\ell_1(z) = 0$ must have a positive root z that satisfies $w_2 = \pm\sqrt{z}$.

To ensure the existence and positivity of w_2 , without loss of generality, we assume that equation (4.15) has three positive real roots, denoted by z_j , $j = 1, 2, 3$. Then, it implies that equation (4.14) has also three real roots which are given by $w_{2j} = \sqrt{z_j}$, $j = 1, 2, 3$.

Now, we proceed to determine the critical value of the time delay τ_2 . To this end, from the first equation of system (4.13), we can get

$$\tau_{2j}^k = \frac{1}{w_{2j}} \arccos\left(\frac{u_2 w_{2j}^2 - u_0}{p}\right) + \frac{2k\pi}{w_{2j}}, \quad (4.16)$$

with $j = 1, 2, 3$, $k = 0, 1, 2, \dots$. Therefore, when $\tau_2 = \tau_{2j}^k$, $j = 1, 2, 3$, $\tau_{20} = \min_{j=1,2,3} \{\tau_{2j}^0\}$ and $w_{20} = w_{2j_0}$, then equation (4.12) has a pair of purely imaginary roots, denoted by $\pm iw_{2j}$.

Next, for this value of τ_{20} , we go to establish the transversality condition of Hopf bifurcation [22, Theorem 1.1, P. 1362] of system (2.1)-(2.2). To do that, let us set

$$\lambda(\tau_2) = \alpha(\tau_2) + iw(\tau_2).$$

Then, do to the fact that λ is root of equation (4.12), we have

$$\alpha(\tau_{20}) = 0, \quad w(\tau_{20}) = w_{20}. \quad (4.17)$$

At this time, using Implicit Function Theorem [23, Theorem 6.8.1, P. 158] and by differentiating both sides of equation (4.12) with respect to τ_2 , we obtain

$$\frac{d\lambda}{d\tau_2} = \frac{\lambda p e^{-\lambda\tau_2}}{3\lambda^2 + 2u_2\lambda + u_1 - \tau_2 p e^{-\lambda\tau_2}}.$$

Hence, we have

$$\left(\frac{d\lambda}{d\tau_2}\right)^{-1} = -\frac{3\lambda^2 + 2u_2\lambda + u_1}{\lambda(\lambda^3 + u_2\lambda^2 + u_1\lambda + u_0)} - \frac{\tau_2}{\lambda}. \quad (4.18)$$

Further, substituting $\lambda = iw_{20}$ and by taking the real part of previous expression (4.18), we obtain

$$\Re\left(\frac{d\lambda}{d\tau_2}\right)^{-1}_{\lambda=iw_{20}} = \frac{3w_{20}^4 + (2u_0u_2 - 4u_1)w_{20}^2 + u_1^2 - 2u_0}{(w_{20}^3 - u_1w_{20})^2 + (u_0 - u_2w_{20}^2)^2}. \quad (4.19)$$

Obviously, we have

$$\begin{aligned} \operatorname{sign}\left\{\frac{d(\Re\lambda)}{d\tau_2}\right\} &= \operatorname{sign}\Re\left\{\left(\frac{d\lambda}{d\tau_2}\right)_{\lambda=iw_{20}}^{-1}\right\} \\ &= \operatorname{sign}\left\{\frac{g_1(w_{20})}{(w_{20}^3 - u_1w_{20})^2 + (u_0 - u_2w_{20}^2)^2}\right\}, \end{aligned}$$

where

$$g_1(w_{20}) = 3w_{20}^4 + (2u_0u_2 - 4u_1)w_{20}^2 + u_1^2 - 2u_0.$$

Therefore, it results that $\Re\left(\frac{d\lambda}{d\tau_2}\right)_{\lambda=iw_{20}}^{-1} > 0$ whenever $g_1(w_{20}) > 0$; which implies that $g_1(w_{20}) > 0$ is an essential condition for the occurrence of Hopf bifurcation of system (2.1) if $\tau_1 = 0$ and $\tau_2 > 0$.

To summarize the above discussion in **Case 2**, we state the following theorem.

Theorem 4.7. *If conditions C4 or C5 holds, then there exists a critical value of the delay time τ_{20} , such that E^* is locally asymptotically stable when $\tau_2 < \tau_{20}$ and unstable when $\tau_2 > \tau_{20}$. Moreover, if $g_1(w_{20}) > 0$, then a Hopf-bifurcation is exhibited by system (2.1)-(2.2) at $\tau_2 = \tau_{20}$.*

Remark 4.8. This result reveals the critical role of the delay parameter τ_2 in shaping the system’s dynamic behavior. The occurrence of a Hopf bifurcation at the threshold value τ_{20} indicates the transition from a stable endemic equilibrium to sustained oscillatory dynamics, corresponding to periodic outbreaks of tuberculosis. From a disease control perspective, such oscillations are undesirable, as they signify recurring waves of infection. Therefore, understanding the bifurcation conditions enables public health policymakers to identify and avoid parameter regimes particularly delay related factors such as diagnostic or treatment delays that lead to instability. Consequently, these findings provide a theoretical foundation for designing intervention strategies aimed at maintaining disease stability and preventing recurrent epidemics.

Case 3: $\tau_1 > 0$ and $\tau_2 = 0$. In this case, the characteristic equation (4.10) turn into

$$c_2\lambda^2 + c_1\lambda + c_0 + p + (\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0)e^{\lambda\tau_1} + (m_1\lambda + m_0)e^{-\lambda\tau_1} = 0. \tag{4.20}$$

Now, suppose that the previous equation has a pure imaginary root $\lambda = iw_1$ with $w_1 > 0$. Then, by inserting it into (4.20) and by taking its real and imaginary parts, we could get

$$\begin{cases} c_2w_1^2 - (c_0 + p) = (-b_2w_1^2 + b_0 + m_0) \cos(w_1\tau_1) + (w_1^3 - b_1w_1 + m_1w_1) \sin(w_1\tau_1), \\ -c_1w_1 = (-w_1^3 + b_1w_1 + m_1w_1) \cos(w_1\tau_1) + (-b_2w_1^2 + b_0 - m_0) \sin(w_1\tau_1). \end{cases}$$

Furthermore, from the previous system, we obtain

$$\begin{cases} \cos(w_1\tau_1) = \frac{Q_{14}w_1^4 + Q_{12}w_1^2 + Q_{10}}{w_1^6 + S_{14}w_1^4 + S_{12}w_1^2 + S_{10}}, \\ \sin(w_1\tau_1) = \frac{Q_{25}w_1^5 + Q_{23}w_1^3 + Q_{21}w_1}{w_1^6 + S_{14}w_1^4 + S_{12}w_1^2 + S_{10}}, \end{cases} \tag{4.21}$$

where

$$\begin{aligned} Q_{14} &= c_1 - c_2b_2, & Q_{12} &= (b_0 - m_0)c_2 + b_2(c_0 + p) - c_1b_1 + c_1m_1, \\ Q_{10} &= -(c_0 + p)(b_0 - m_0), & S_{14} &= b_2^2 - 2b_1, & S_{12} &= -2b_2b_0 + b_1^2 - m_1^2, \\ S_{10} &= b_0^2 - m_0^2, & Q_{25} &= c_2, & Q_{23} &= -b_1c_2 - m_1c_2 - (c_0 + p) + c_1b_2, \\ Q_{21} &= (c_0 + p)(b_1 + m_1) - c_1b_0 - c_1m_0. \end{aligned}$$

After that, by squaring equations of system (4.21) and combining them, we get

$$w_1^{12} + h_{10}w_1^{10} + h_8w_1^8 + h_6w_1^6 + h_4w_1^4 + h_2w_1^2 + h_0 = 0, \tag{4.22}$$

where

$$\begin{aligned}
 h_{10} &= 2S_{14} - Q_{25}^2, \\
 h_8 &= S_{14}^2 + 2S_{12} - 2Q_{25}Q_{23} - Q_{14}^2, \\
 h_6 &= 2S_{10} + 2S_{14}S_{12} - Q_{23}^2 - 2Q_{25}Q_{21} - 2Q_{14}Q_{12}, \\
 h_4 &= S_{12}^2 + 2S_{14}S_{10} - 2Q_{23}Q_{21} - Q_{12}^2 - 2Q_{14}Q_{10}, \\
 h_2 &= 2S_{12}S_{10} - Q_{21}^2 - 2Q_{12}Q_{10}, \\
 h_0 &= S_{10}^2 - Q_{10}^2.
 \end{aligned}$$

At this point, by setting $z_1 = w_1^2$, equation (4.22) can be expressed as follows

$$\ell_2(z_1) = z_1^6 + h_{10}z_1^5 + h_8z_1^4 + h_6z_1^3 + h_4z_1^2 + h_2z_1 + h_0 = 0. \tag{4.23}$$

Next, through the use of Intermediate Value Theorem, if $h_0 < 0$, then equation (4.23) has a positive root z_1 satisfying $w_1 = \pm\sqrt{z_1}$.

Without loss of generality, we assume that equation $\ell_2(z_1) = 0$ has several positive real roots denoted by z_{1j} , $j = 1, 2, \dots, 6$, which implies that equation (4.22) also has multiple real roots $w_{1j} = \sqrt{z_{1j}}$, $j = 1, 2, \dots, 6$.

Latterly, we pass to establish the critical value of time delay τ_{10} . To do this, from the first equation of system (4.21), it yields that

$$\tau_{1j}^k = \frac{1}{w_{1j}} \arccos \left(\frac{Q_{14}w_{1j}^4 + Q_{12}w_{1j}^2 + Q_{10}}{w_{1j}^6 + S_{14}w_{1j}^4 + S_{12}w_{1j}^2 + S_{10}} \right) + \frac{2k\pi}{w_{1j}}, \tag{4.24}$$

with $j = 1, 2, \dots, 6$, $k = 1, 2, \dots$. Therefore, when $\tau_1 = \tau_{1j}^k$, $j = 1, 2, \dots, 6$, with $\tau_{10} = \min_{j=1,2,\dots,6} \{\tau_{1j}^0\}$ and $w_{10} = w_{1j_0}$, the equation (4.20) admits a pair of purely imaginary roots $\pm iw_{1j}$.

For the bifurcation analysis, the time delay τ_1 is chosen as the bifurcation parameter and we will show that there exists at least one root with positive real part for $\tau_1 > \tau_{10}$.

With help of Implicit Function Theorem [23, Theorem 6.8.1, P. 158] and by differentiating equation (4.20), it leads to obtain

$$\left(\frac{d\lambda}{d\tau_1} \right)^{-1} = \frac{(2c_2\lambda + c_1) + (3\lambda^2 + 2b_2\lambda + b_1)e^{\lambda\tau_1} + m_1e^{-\lambda\tau_1}}{\lambda(c_2\lambda^3 + c_1\lambda^2 + c_0 + p)e^{\lambda\tau_1} - 2\lambda(m_1\lambda + m_0)e^{-\lambda\tau_1}} - \frac{\tau_1}{\lambda}. \tag{4.25}$$

Moreover, if we replace λ with iw_{10} and extract the real component from the preceding equation (4.25), we can get

$$\Re \left(\frac{d\lambda}{d\tau_1} \right)^{-1}_{\lambda=iw_{10}} = \frac{g_2(w_{10})}{\xi_1^2 + \xi_2^2}, \tag{4.26}$$

where

$$g_2(w_{10}) = \zeta_5w_{10}^5 + \zeta_4w_{10}^4 + \zeta_3w_{10}^3 + \zeta_2w_{10}^2 + \zeta_1w_{10}, \tag{4.27}$$

with,

$$\begin{aligned} \zeta_5 &= 3c_2 \sin(w_{10}\tau_1), \\ \zeta_4 &= -2c_2^2 + (3c_1 - 2c_2b_2) \cos(w_{10}\tau_1) + 6m_1(\cos^2(w_{10}\tau_1) - \sin^2(w_{10}\tau_1)), \\ \zeta_3 &= (2c_1b_2 + 5c_2m_1 - 3(c_0 + p) - b_1c_2) \sin(w_{10}\tau_1) \\ &\quad + (8m_1b_2 - 12m_0) \cos(w_{10}\tau_1) \sin(w_{10}\tau_1), \\ \zeta_2 &= -c_1^2 + 2c_2(c_0 + p) - 2m_1^2 + (4b_2m_0 - 2m_1b_1)(\sin^2(w_{10}\tau_1) - \cos^2(w_{10}\tau_1)) \\ &\quad + (-3m_1c_1 - b_1c_1 + 4c_2m_0 + 2b_2(c_0 + p)) \cos(w_{10}\tau_1), \\ \zeta_1 &= (2c_1m_0 - m_1(c_0 + p) + b_1(c_0 + p)) \sin(w_{10}\tau_1) + 4b_1m_0 \cos(w_{10}\tau_1) \sin(w_{10}\tau_1), \\ \xi_1 &= -c_1w_{10}^2 - 2m_1w_{10}^2 \cos(w_{10}\tau_1) + 2m_0w_{10} \sin(w_{10}\tau_1), \\ \xi_2 &= -c_2w_{10}^3 + 2m_1w_{10}^2 \sin(w_{10}\tau_1) + (c_0 + p)w_{10} + 2m_0w_{10} \cos(w_{10}\tau_1). \end{aligned}$$

Thus, an essential condition for the occurrence of Hopf-bifurcation which is $g_2(w_{10}) > 0$. From above, we can conclude the following result.

Theorem 4.9. *Let h_0 given in (4.22), If $h_0 < 0$ is satisfied, then there exists a critical value of the time delay τ_{10} , such that the endemic equilibrium E^* is locally asymptotically stable when $\tau_1 < \tau_{10}$ and it is unstable if $\tau_1 > \tau_{10}$. Moreover, if $g_2(w_{10}) > 0$, then Hopf-bifurcation is exhibited by the system at $\tau_1 = \tau_{10}$.*

Case 4: $\tau = \tau_1 = \tau_2$ where $\tau > 0$. In this case, equation (4.10) becomes as follows

$$(\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0)e^{\lambda\tau} + (m_1\lambda + m_0 + p)e^{-\lambda\tau} + c_2\lambda^2 + c_1\lambda + c_0 = 0. \tag{4.28}$$

Proceeding in the same way as before. First, we suppose that $\lambda = iw$, ($w > 0$) is a root of equation (4.28), then we could obtain

$$-c_2w^2 + ic_1w + c_0 + (-iw^3 - b_2w^2 + ib_1w + b_0)e^{iw\tau} + (im_1w + (m_0 + p))e^{-iw\tau} = 0.$$

Next, we take the real and imaginary parts of previous equations, to get the following system

$$\begin{cases} (-b_2w^2 + b_0 + m_0 + p) \cos w\tau + (w^3 - b_1w + m_1w) \sin w\tau = c_2w^2 - c_0, \\ (-w^3 + b_1w + m_1w) \cos w\tau + (-b_2w^2 + b_0 - (m_0 + p)) \sin w\tau = -c_1w. \end{cases} \tag{4.29}$$

Further, from system (4.29), we find

$$\begin{cases} \cos(w\tau) = \frac{B_{14}w^4 + B_{12}w^2 + B_{10}}{w^6 + A_{14}w^4 + A_{12}w^2 + A_{10}}, \\ \sin(w\tau) = \frac{B_{25}w^5 + B_{23}w^3 + B_{21}w}{w^6 + A_{14}w^4 + A_{12}w^2 + A_{10}}, \end{cases} \tag{4.30}$$

where

$$\begin{aligned} B_{14} &= -c_2b_2 + c_1, \quad B_{12} = c_2(b_0 - (m_0 + p)) + c_0b_2 + b_1c_1 + c_1m_1, \\ B_{10} &= c_0(b_0 - (m_0 + p)), \quad A_{14} = b_2^2 - 2b_1, \\ A_{12} &= b_1^2 - m_1^2 - 2b_0b_2, \quad A_{10} = b_0^2 - (m_0 + p)^2, \\ B_{25} &= c_2, \quad B_{23} = -c_0 + c_1b_2 - c_2(b_1 + m_1), \\ B_{21} &= -b_0c_1 - c_1(m_0 + p) + c_0(b_1 + m_1). \end{aligned}$$

Later, we square and we add the equations of system (4.30), we arrive at

$$w^{12} + k_{10}w^{10} + k_8w^8 + k_6w^6 + k_4w^4 + k_2w^2 + k_0 = 0, \tag{4.31}$$

where

$$\begin{aligned} k_{10} &= 2A_{14} - B_{25}^2, \\ k_8 &= A_{14}^2 + 2A_{12} - 2B_{25}B_{23} - B_{14}^2, \\ k_6 &= 2A_{10} + 2A_{14}A_{12} - B_{23}^2 - 2B_{25}B_{21} - 2B_{14}B_{12}, \\ k_4 &= A_{12}^2 + 2A_{14}A_{10} - 2B_{23}B_{21} - B_{12}^2 - 2B_{14}B_{10}, \\ k_2 &= 2A_{14}A_{10} - B_{21}^2 - 2B_{12}B_{10}, \\ k_0 &= A_{10}^2 - B_{10}^2. \end{aligned}$$

At this stage, we consider that $z_4 = w^2$ and we obtain

$$\ell_3(z_4) = z_4^6 + k_{10}z_4^5 + k_8z_4^4 + k_6z_4^3 + k_4z_4^2 + k_2z_4 + k_0 = 0. \quad (4.32)$$

By using Intermediate Value Theorem again, we can show that equation (4.32) has a positive real root z_4 satisfying $w = \pm\sqrt{z_4}$. Without loss of generality, we assume that $\ell_3(z_4) = 0$ has six positive real roots z_{4j} , $j = 1, 2, \dots, 6$, which implies that equation (4.31) also has six real roots $w_j = \sqrt{z_{4j}}$, $j = 1, 2, \dots, 6$.

Now, from the first equation of system (4.30), we obtain

$$\tau_j^k = \frac{1}{w_j} \arccos \left(\frac{B_{14}w_j^4 + B_{12}w_j^2 + B_{10}}{w_j^6 + A_{14}w_j^4 + A_{12}w_j^2 + A_{10}} \right) + \frac{2k\pi}{w_j}, \quad (4.33)$$

with $j = 1, 2, \dots, 6$, $k = 0, 1, 2, \dots$. Therefore, $\pm iw_j$ is a pair of purely imaginary roots of equation (4.28), when $\tau = \tau_j^k$, with $\tau_0 = \min_{j=1,2,\dots,6} \{\tau_j^0\}$ and $w_0 = w_{j_0}$.

To determine the condition of Hopf-Bifurcation occurs for the critical value of τ , we will use the derivative equation (4.28) concerning τ ; we obtain

$$\frac{d\lambda}{d\tau} = \frac{-\lambda \left((\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0)e^{\lambda\tau} - (m_1\lambda + m_0 + p)e^{-\lambda\tau} \right)}{(2c_2\lambda + c_1) + (3\lambda^2 + 2b_2\lambda + b_1)e^{\lambda\tau} + m_1e^{-\lambda\tau} + \tau \left((\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0)e^{\lambda\tau} - (m_1\lambda + m_0 + p)e^{-\lambda\tau} \right)},$$

which leads to

$$\left(\frac{d\lambda}{d\tau} \right)^{-1} = \frac{(2c_2\lambda + c_1) + (3\lambda^2 + 2b_2\lambda + b_1)e^{\lambda\tau} + m_1e^{-\lambda\tau}}{-\lambda \left((\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0)e^{\lambda\tau} - (m_1\lambda + m_0 + p)e^{-\lambda\tau} \right)} - \frac{\tau}{\lambda}. \quad (4.34)$$

Next, substituting $\lambda = iw_0$ in (4.34), and by taking its real part, we can get

$$\Re \left(\frac{d\lambda}{d\tau} \right)^{-1}_{\lambda=iw_0} = \frac{g_3(w_0)}{\xi_3^2 + \xi_4^2}, \quad (4.35)$$

where

$$g_3(w_0) = 3w_0^6 + \eta_5w_0^5 + \eta_4w_0^4 + \eta_3w_0^3 + \eta_2w_0^2 + \eta_1w_0, \quad (4.36)$$

with,

$$\eta_5 = 3c_2 \sin(w_0\tau),$$

$$\eta_4 = -2c_2^2 + (3c_1 - 2c_2b_2) \cos(w_0\tau) + 6m_1 (\cos^2(w_1\tau)) - \sin^2(w_1\tau),$$

$$\eta_3 = (2c_1b_2 + 5c_2m_1 - 3c_0 - b_1c_2) \sin(w_0\tau) + (8m_1b_2 - 12(m_0 + p)) \cos(w_0\tau) \sin(w_0\tau),$$

$$\begin{aligned} \eta_2 &= -c_1^2 + 2c_2c_0 - 2m_1^2 + (4b_2(m_0 + p) - 2m_1b_1) (\sin^2(w_0\tau) - \cos^2(w_0\tau)) \\ &\quad + (-3m_1c_1 - b_1c_1 + 4c_2(m_0 + p) + 2b_2(c_0 + p)) \cos(w_0\tau), \end{aligned}$$

$$\eta_1 = (2c_1(m_0 + p) - m_1c_0 + b_1c_0) \sin(w_0\tau) + 4b_1(m_0 + p) \cos(w_0\tau) \sin(w_0\tau),$$

$$\xi_3 = -c_1w_0^2 - 2m_1w_0^2 \cos(w_0\tau) + 2m_0w_{10} \sin(w_0\tau),$$

$$\xi_4 = -c_2w_{10}^3 + 2m_1w_0^2 \sin(w_0\tau) + (c_0 + p)w_0 + 2m_0w_0 \cos(w_0\tau).$$

Hence, we can conclude that if $\tau_1 = \tau_2 = \tau$, the occurrence of Hopf bifurcation in system (2.1)-(2.2) requires the essential condition of $g_3(w_0) > 0$. This condition is supported by the fact that $\Re\left(\frac{d\lambda}{d\tau}\right)^{-1}_{\lambda=iw_0} > 0$ holds true in such cases. The following result describes the conditions for Hopf bifurcation at the endemic equilibrium.

Theorem 4.10. For $\tau_1 = \tau_2 = \tau$ ($\tau > 0$), if k_0 , which is given in equation (4.31), satisfies $k_0 < 0$, then there exists a critical value of delay time τ_0 , such that the endemic equilibrium point E^* is locally asymptotically stable for $\tau < \tau_0$ and is unstable for $\tau > \tau_0$. Also, if $g_3(w_0) > 0$, Hopf-bifurcation is exhibited by the system at $\tau = \tau_0$.

5 Numerical simulation

We numerically solve the system using the parameter values from Table 1 in order to validate the analytical results.

Table 1: Parameters values.

Parameter	Value	Unit	source
Π	20	day ⁻¹	[24]
β_1	0.001	day ⁻¹	variable
β_2	0.3	day ⁻¹	variable
μ_I	0.1	day ⁻¹	[24]
μ	0.02	day ⁻¹	[24]
σ	0.1	day ⁻¹	variable
α	0.4	day ⁻¹	variable

The initial conditions are taken as $S(0) = 200$, $I(0) = 75$, and $R(0) = 55$. For these values, the disease-free equilibrium point is computed as $E^0 = (1000, 0, 0)$. It is not difficult to calculate the value of \mathcal{R}_0 , which is $\mathcal{R}_0 = 0.4200$. Since \mathcal{R}_0 is less than 1, the roots of equation (4.3) have negative real parts. Therefore, E^0 is locally asymptotically stable for $\mathcal{R}_0 < 1$ with $\tau_1, \tau_2 > 0$. Additionally, Figure 1 confirms the Remark 4.4 that the stability of the disease-free equilibrium point does not depend on the time delays τ_1 and τ_2 .

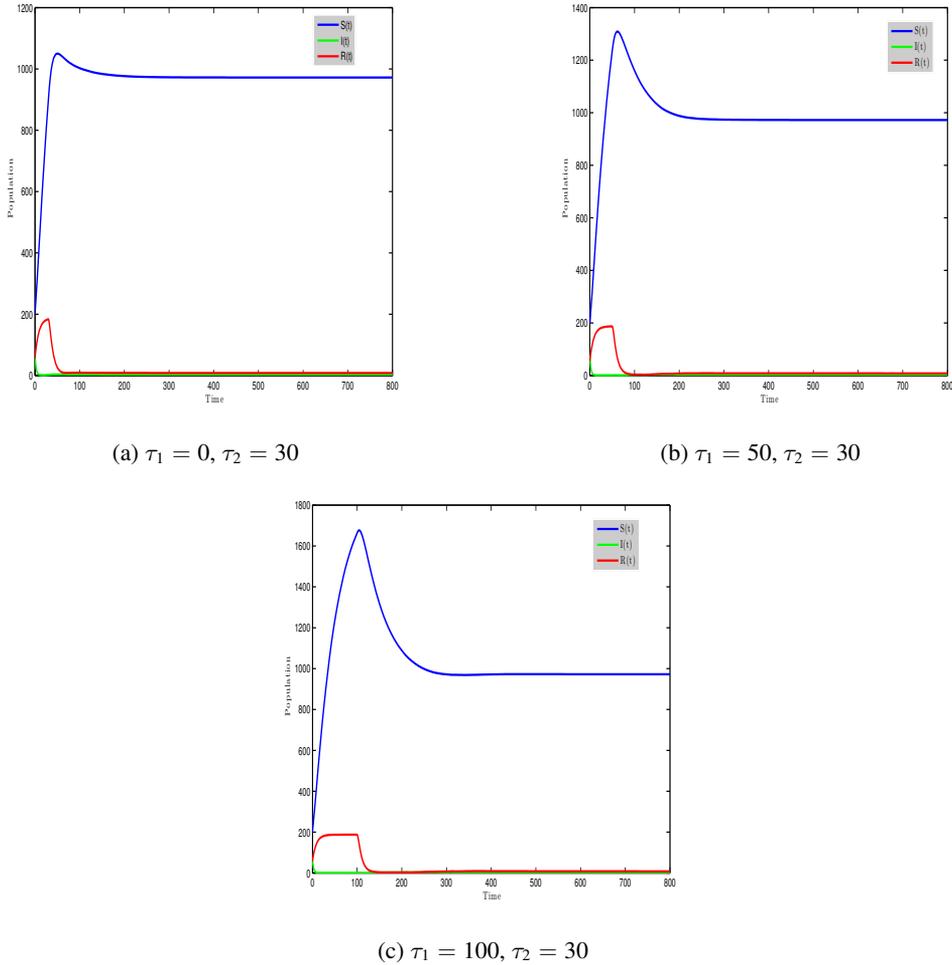


Figure 1: Graphical Analysis of Local Asymptotic Stability for Disease-Free Equilibrium Point $E_0 = (1000, 0, 0)$, with $\mathcal{R}_0 = 0.4200 < 1$, under Varying τ_1 Values.

Case 1: For the case of $\tau_1 = \tau_2 = 0$, we select the parameters β_1 , β_2 , and σ as follows

$$\beta_1 = 0.06, \quad \beta_2 = 0.01 \quad \text{and} \quad \sigma = 0.001. \quad (5.1)$$

When we substitute these values, we find that $\mathcal{R}_0 = 7.8000 > 1$. This condition is crucial for the existence and nonnegativity of the endemic equilibrium point $E^* = \left(\frac{277420}{2313}, \frac{209545}{1542}, \frac{149675}{2313} \right)$. Additionally, it should be noted that with the values provided by (5.1), the condition $C0$ $q_1 = 0.3158 > 0$, $q_3 = 9.0173 \times 10^{-4} > 0$, and $q_1 q_2 - q_3 = 0.0146 > 0$ are all satisfied. Therefore, based on Theorem 4.5, we can conclude that the endemic equilibrium point E^* is locally asymptotically stable when $\tau_1 = \tau_2 = 0$ (see Figure 2).

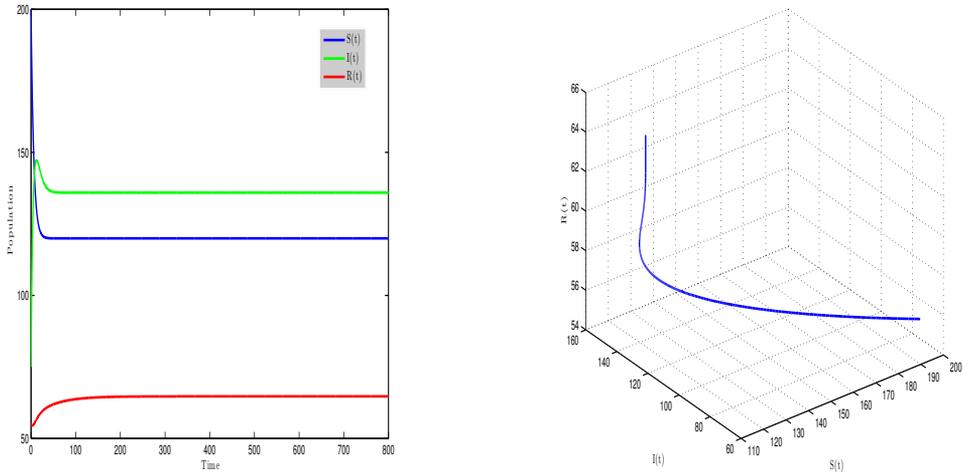


Figure 2: Graphs justifying the local asymptotic stability of endemic equilibrium point with absence of delay times τ_1 and τ_2 .

Case 2: When $\tau_1 = 0$ and $\tau_2 > 0$. To investigate this case, we choose

$$\beta_1 = 0.00162, \quad \beta_2 = 0.6, \quad \sigma = 0.6 \quad \text{and} \quad \alpha = 0.0001. \tag{5.2}$$

Consequently, $\mathcal{R}_0 = 1.1664 > 1$ and the endemic equilibrium point E^* is given by $E^* = \left(\frac{2191000}{4891}, \frac{387500}{4891}, \frac{375000}{4891} \right)$.

By solving the equation (4.15) we find that $-0.3693, 0.0714, -0.0758$ are the roots. Thus we obtain one positive roots of equation (4.14), $w = 0.2672$. Consequently, $\tau_2 = 10.8916$. Since $\tau_{20} = \min_{j=1,2,3} \{\tau_2^j\}$, we have then $\tau_{20} = 10.8916$. Figure 3 provides evidence for the local stability of the endemic equilibrium point when $\tau_2 = 10$, which is less than τ_{20} . On the other hand, Figure 4 illustrates the instability when $\tau_2 = 11$, surpassing τ_{20} .

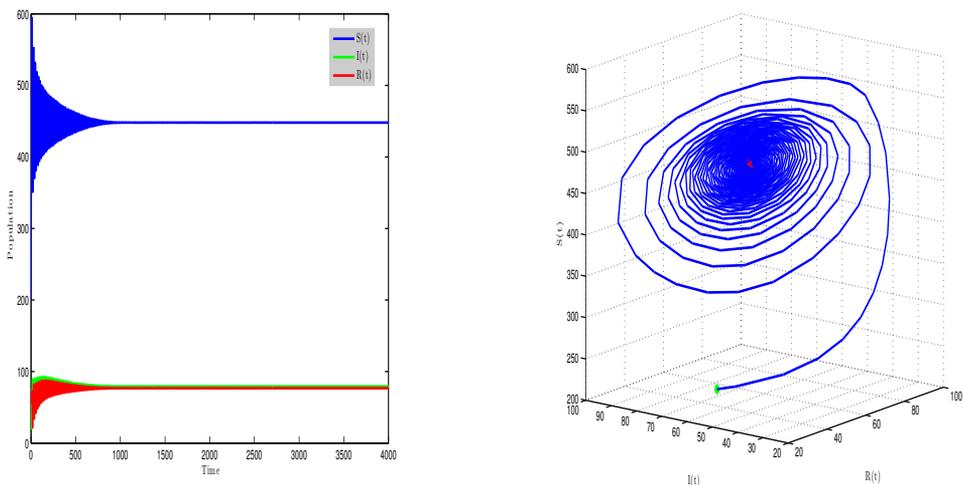


Figure 3: The graphs demonstrate that the endemic equilibrium point E^* exhibits local asymptotic stability when $\tau_2 < \tau_{20}$.

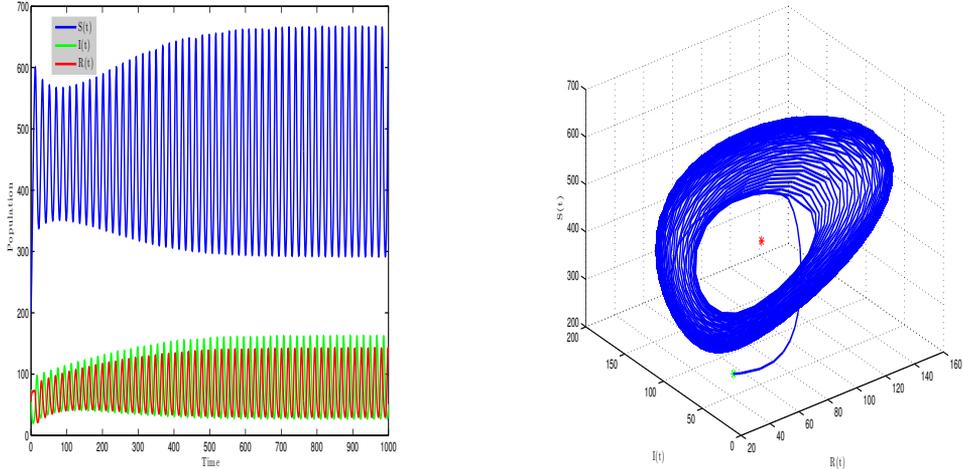


Figure 4: Graphs justifying that the endemic equilibrium point E^* is unstable when $\tau_2 > \tau_{20}$.

Case 3: the case when $\tau_1 > 0, \tau_2 = 0$, we choose $\beta_1 = 0.013, \beta_2 = 0.001, \sigma = 0.01$ and $\alpha = 0.3$. then we obtain that $\mathcal{R}_0 = 1.5730 > 1$, it means the endemic equilibrium point E^* exist which is $E^* = (\frac{1110901}{3442}, \frac{193185}{1721}, \frac{12879}{3442})$. Moreover, the condition $h_0 = -4.4772 \times 10^{-18} < 0$ is satisfied at the positive equilibrium point E^* and with simple calculation we get $\tau_{10} = 58.6921$. Then the endemic equilibrium point E^* is locally asymptotically stable when $\tau_1 < \tau_{10} = 56$ and it is unstable when $\tau_1 > \tau_{10} = 60$, which is consistent with Theorem 4. Figure 5a and Figure 5b as show that.

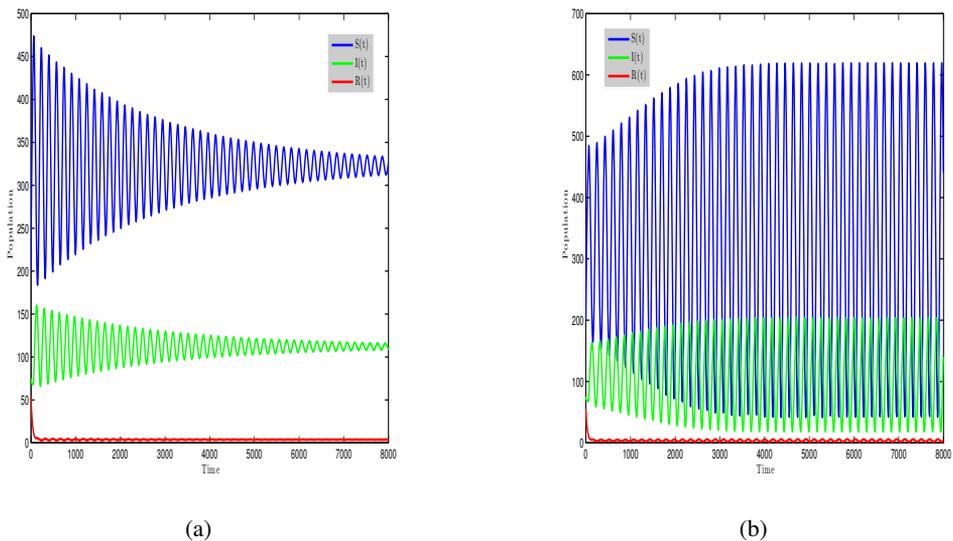


Figure 5: Graphs justifying the local asymptotic stability of E^* when $\tau_1 = 13 < \tau_{10}$ (a). (b) When $\tau_1 = 14.2 > \tau_{10}$, E^* is unstable.

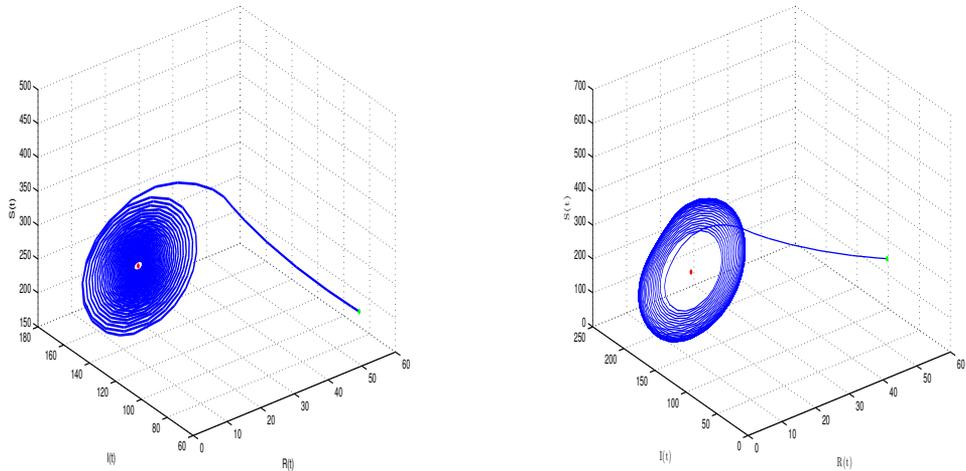


Figure 6: 3-dimensional visualization of the solution trajectory.

Case 4: $\tau_1 = \tau_2 = \tau$, we choose $\beta_1 = 0.06$, $\beta_2 = 0.02$, $\sigma = 0.2$ and $\alpha = 0.6$, we get $\mathcal{R}_0 = 8.4000$ and the equilibrium point $E^* = (\frac{697690}{2703}, \frac{329230}{2703}, \frac{29930}{2703})$. We calculate that the characteristic equation for the matrix J^* evaluated at E^* is

$$0.0648\lambda^2 + 0.0235\lambda + 0.002 + (\lambda^3 + 0.38\lambda^2 + 0.038\lambda + 6.16 \times 10^{-04})e^{\lambda\tau} + (0.0043\lambda + 6.7753 \times 10^{-04})e^{-\lambda\tau} = 0.$$

suppose that the characteristic equation has a purely imaginary root $\lambda = iw$. After separating real and imaginary parts and substituting $z_4 = w^2$ in equation (4.32)

$$z_4^6 + 0.1326z_4^5 + 0.0032z_4^4 + 2.3851 \times 10^{-04}z_4^3 + 1.8032 \times 10^{-08}z_4^2 - 2.9340 \times 10^{-09}z_4 - 9.2545 \times 10^{-15} = 0. \tag{5.3}$$

The condition $k_0 < 0$ is satisfied, and the roots of equation (5.3) are -0.1224 , $-0.0050 + 0.0439i$, $-0.0050 - 0.0439i$, -0.0036 , 0.0034 . Then we get $\tau_0 = 10.6575$. From Figure 7a, it can be observed that for $\tau = 10$, the trajectories corresponding to $S(t)$, $I(t)$, and $R(t)$ initially vary before converging towards the respective components of the equilibrium point E^* . Figure 7b illustrates how the solution trajectory, starting from the initial condition, converges towards $(258.11690, 121.80170, 11.07288)$. While for $\tau = 11$, the solution trajectories begin oscillating continuously around the equilibrium point, which supports the existence of Hopf-bifurcation. We can witness E^* is unstable behavior for $\tau = 11$. further from Figure 8, we can see the unstable behavior of E^* for $\tau = 11$. Thus, the endemic equilibrium point E^* is locally asymptotically stable for $\tau \in [0, 10.6575)$ and becomes unstable for $\tau > 10.6575$.

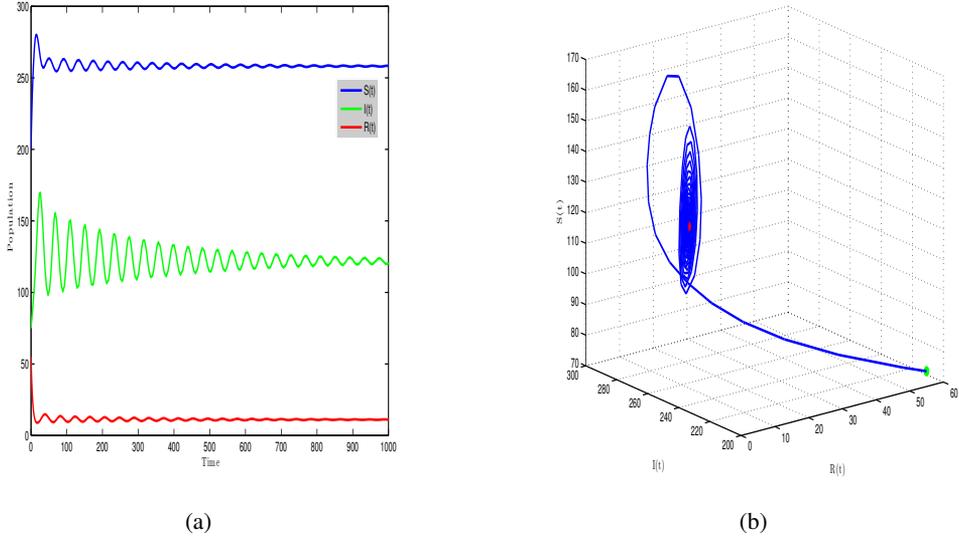


Figure 7: Graphs justifying the local asymptotic stability of the endemic equilibrium point E^* when $\tau = 10$. (b) 3-dimensional visualization of the solution trajectory.

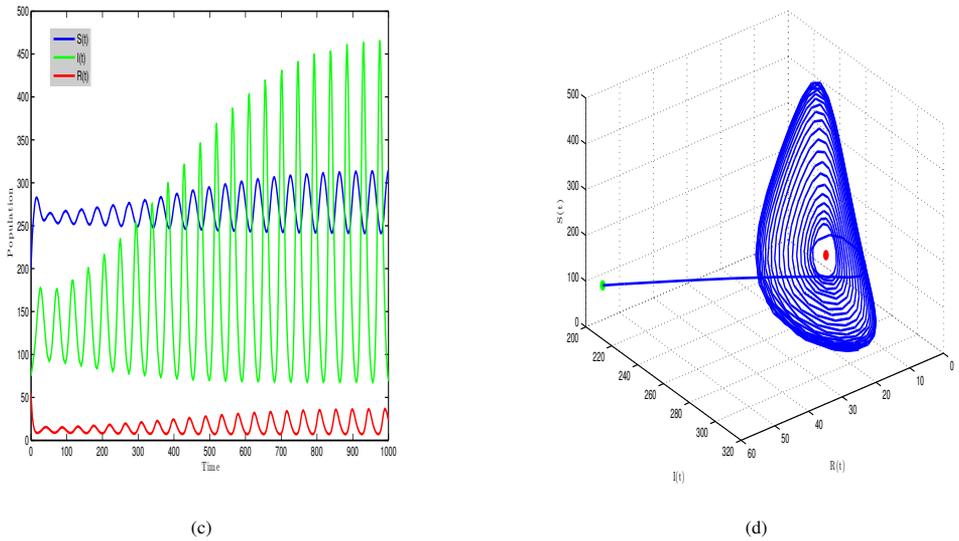
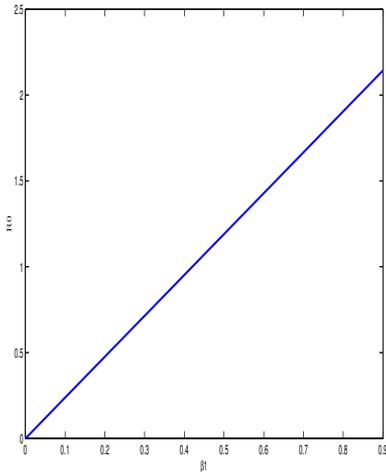
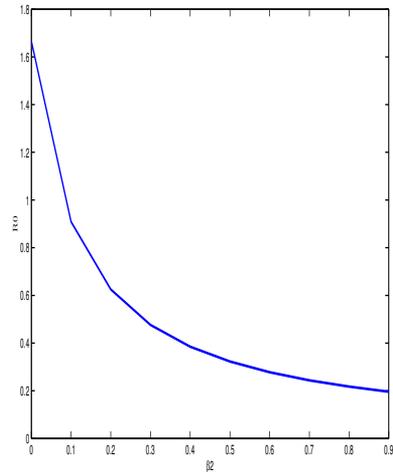


Figure 8: (c) When $\tau = 11 > \tau_0$, E^* is unstable. (d) 3-dimensional visualization of the solution trajectory.

Now, To confirm the results obtained in Remark 4.3, we can demonstrate them through numerical simulation. We show how \mathcal{R}_0 relates to parameters β_1 and β_2 . Figure 9a show the direct proportion relationship between \mathcal{R}_0 and β_1 we find that as β_1 increases, \mathcal{R}_0 increases too, and as shown in Figure 9b the inverse relationship between \mathcal{R}_0 and β_2 . Moreover, when we choose $\mu = 0.02$, $\mu_I = 0.1$, $(\beta_1, \beta_2) \in [0, 0.9] \times [0, 0.9]$, as shown in Figure 10 we conclude the relationship among \mathcal{R}_0 , β_1 , β_2 . It demonstrates that as β_1 increases and β_2 decreases, \mathcal{R}_0 is gradually increasing. High frequency of exposure between vulnerable individuals and low recovery rates and sick people make epidemic diseases more likely to spread.



(a) The relationship between \mathcal{R}_0 and β_1 .
Parameters: $\mu = 0.02, \mu_1 = 0.1, \beta_2 = 0.3$.



(b) The relationship between \mathcal{R}_0 and β_2 .
Parameters: $\mu = 0.02, \mu_1 = 0.1, \beta_1 = 0.2$.

Figure 9: The relationship between \mathcal{R}_0 and parameters.

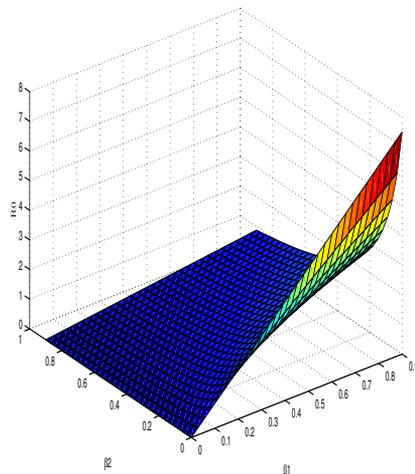


Figure 10: The relationship among \mathcal{R}_0, β_1 , and β_2 .

6 Conclusion

This paper analyses a mathematical model used to study tuberculosis infection, focusing on two distinct time delays. The first delay, denoted as τ_1 , represents the period between the appearance of symptoms and the diagnosis of the disease. The second delay, τ_2 , refers to the interval before initiating appropriate treatment. Both delays play crucial roles in the transmission dynamics of tuberculosis. τ_1 is vital for early diagnosis, which directly impacts the effectiveness of intervention measures. In contrast, τ_2 pertains to the delay in starting treatment, which is key to controlling the spread and progression of the disease. Additionally, we examined the effects of these time delays in the framework of bifurcation analysis. The time delays τ_1 and τ_2 are instrumental in defining the conditions under which Hopf bifurcation occurs, influencing the stability of the disease-free state and the endemic equilibrium of tuberculosis in the population. Our results highlight the importance of these delays in shaping the overall dynamics and stability of tuberculosis transmission.

The study has great potential for real-world application in public health, particularly in optimizing tuberculosis control strategies. The incorporation of time delays in the model mirrors the real-world delay in diagnosis and treatment. The findings could help health authorities understand how delays impact the stability of tuberculosis transmission and guide interventions aimed at reducing such delays.

In conclusion, this study's findings underscore the critical importance of early diagnosis and timely treatment in managing tuberculosis. Prompt detection of symptoms and the rapid initiation of appropriate therapy are essential for reducing the disease burden and preventing further transmission and progression. These results emphasize the necessity for efficient public health strategies that promote early diagnosis and swift treatment, aiming to reduce the overall impact of tuberculosis on public health.

References

- [1] World Health Organization. <http://www.who.int/mediacentre/factsheets/fs104/en/>
- [2] H. Waaler, A. Geser, & S. Andersen, The use of mathematical models in the study of the epidemiology of tuberculosis., *Am. J. Public Health Nations Health*, **52**(6), (1962), 1002–1013.
- [3] Y. Yang, J. Li, Z. Ma, & L. Liu, Global stability of two models with incomplete treatment for tuberculosis., *Chaos Solitons Fractals*, **43**(1–12), (2010), 79–85.
- [4] I. Ullah, S. Ahmad, Q. Al-Mdallal, Z. A. Khan, H. Khan, & A. Khan, Stability analysis of a dynamical model of tuberculosis with incomplete treatment., *Adv. Differ. Equ.*, **2020**(499), (2020), 1–14.
- [5] D. P. Moualeu, S. Bowong, & Y. Emvudu, Extended hypergeometric functions of two and three variables, *J. Appl. Math. & Informatics*, **29**(5-6), (2011), 1097–1115 .
- [6] S. Das, T. Sarkar & P. Biswas, Extended hypergeometric functions of two and three variables, *Phys. Scr.*, **100**(1), No. 015271, (2025).
- [7] K. Shah, T. Abdeljawad, B. Abdalla, & M. S. Abualrub, Utilizing fixed point approach to investigate piecewise equations with non-singular type derivative, *Aims Math*, **7**(8), (2022), 14614–14630.
- [8] A. Aghriche, Mathematical Model of COVID-19 Transmission with Education Campaign and Treatment Through Quarantine, *Palestine Journal of Mathematics.*, **14**(1), (2025), 142–154.
- [9] Z. Feng, C. Castillo-Chavez, & A. F. Capurro, A model for tuberculosis with exogenous reinfection, *Theor. Popul. Biol.*, **57**(3), (2000), 235–247.
- [10] M. M. Ojo, O. J. Peter, E. F. D. Goufo et al., Mathematical model for control of tuberculosis epidemiology, *J. Appl. Math. Comput.*, **69**, (2023), 69–87.
- [11] K. Shah, H. Naz, T. Abdeljawad, B. Abdalla, Study of fractional order dynamical system of viral infection disease under piecewise derivative, *CMES-Comput. Model. Eng. Sci.*, **136**(1), (2023).
- [12] T. Abdeljawad, K. Shah, M. S. Abdo, & F. Jarad, An analytical study of fractional delay impulsive implicit systems with Mittag-Leffler law, *Appl. Comput. Math.*, **22**(1), (2023), 31–44.
- [13] H. Agarwal, M. N. Mishra & R. S. Dubey, Exploring a Mathematical Model for the Interaction Between Cancer Cells and Virotherapy Utilizing Fractional Derivative, *Palestine Journal of Mathematics.*, **14**(1), (2022), 694–706.
- [14] L. Perko, *Differential Equations and Dynamical Systems*, Springer Science & Business Media, **Vol. 7**, (2013).
- [15] S. H. Strogatz, *Nonlinear Dynamics and Chaos: With Applications to Physics, Biology, Chemistry, and Engineering*, CRC Press, (2018).
- [16] J. Z. Zhang, Z. Jin, Q. X. Liu, Z. Y. Zhang, Analysis of a delayed SIR model with nonlinear incidence rate, *Discrete Dyn. Nat. Soc.*, (2008).
- [17] C. Castillo-Chavez, & B. Song, Dynamical models of tuberculosis and their applications, *Math. Biosci. Eng.*, **1**(2), (2004), 361–404.
- [18] W. Rudin, *Principles of Mathematical Analysis*, (Third Ed.), New York, McGraw-Hill, (1976).
- [19] R. Morgan, Linearization and stability analysis of nonlinear problems, *Rose-Hulman Undergrad. Math. J.*, **16**(2), Art. 5, (2015).
- [20] J. Yu, & M. Peng, Stability and bifurcation analysis for the Kaldor–Kalecki model with a discrete delay and a distributed delay, *Physica A*, **460**, (2016), 66–75.
- [21] J.J. Anagnost, & C.A. Desoer, An elementary proof of the Routh–Hurwitz stability criterion, *Circuits Syst. Signal Process.*, **10**(1), (1991), 101–114.
- [22] K. Gatermann, M. Eiswirth, & A. Sensse, Toric ideals and graph theory to analyze Hopf bifurcations in mass action systems, *J. Symb. Comput.*, **40**(6), (2005), 1361–1382.

[23] T. Tao, Analysis II, (Third Ed.), Springer, (2016).

[24] Tanvi, R. Aggarwal, Stability analysis of a delayed HIV-TB co-infection model in resource limitation settings, *Chaos Solitons Fractals*, **140**, Art. 110138, (2020).

Appendix A

Lemma .1.

- (i) If C1, C2 or C3 holds, then equation (4.15) has no positive real roots.
- (ii) If C4 or C5 holds, then equation (4.15) has at least one positive real root.

Proof. Firstly, we need to show that under the conditions stated in C1, C2 or C3, the function $\ell_1(z) = 0$ given by (4.15) does not have any positive real roots.

Let's consider the derivative $\ell'_1(z)$ and analyze its behavior. If $\ell'_1(z) > 0$ for all $z > 0$, then $\ell_1(z)$ is strictly increasing and cannot have any positive real roots. Indeed, from the condition C1, it follows that $\ell'_1(z) > 0$ for all $z > 0$ which implies that function $\ell_1(z)$ is strictly increasing for all $z > 0$ (see Figure 11).

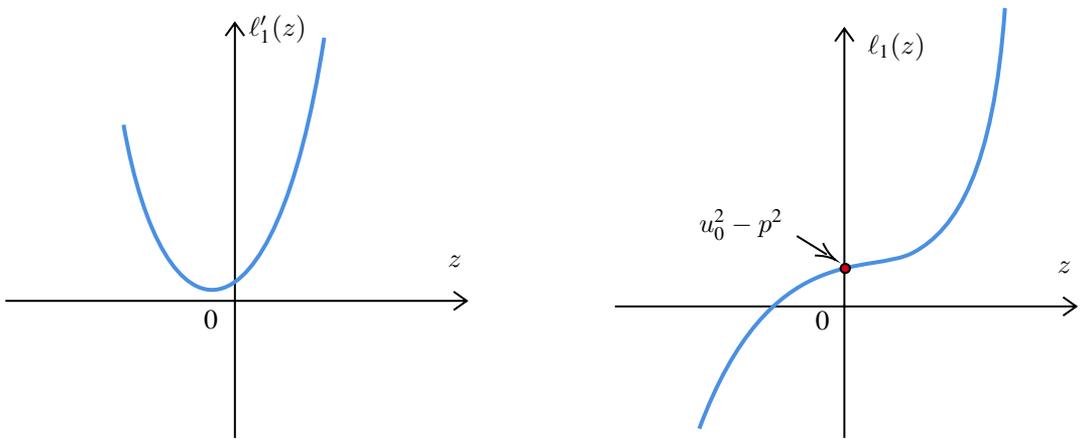


Figure 11: $u_0^2 - p^2 \geq 0, \Delta_{\ell'_1} \leq 0$.

By the same way as before, we can easily see that function $\ell_1(z)$ does not admit a positive root for all $z > 0$ under the condition C2 (see Figure 12).

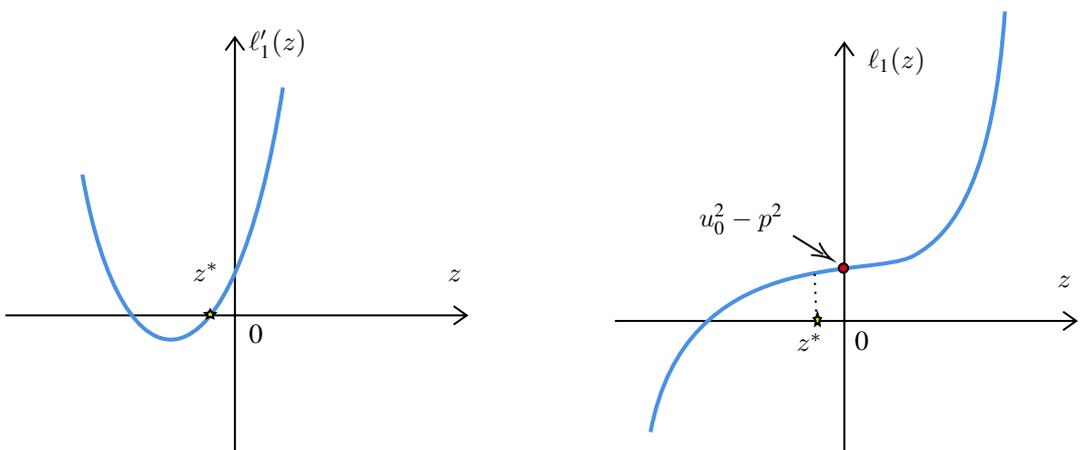


Figure 12: $u_0^2 - p^2 \geq 0, \Delta_{\ell'_1} \geq 0, z^* < 0$.

Now, if the condition C3 is satisfied, then the function ℓ_1 is increasing on $(0, z^*)$ and goes from $\ell_1(0) = u_0^2 - p^2 \geq 0$ to $\ell_1(z^*) > 0$; however, the function $\ell_1(z)$ is decreasing for all $z > z^*$. This

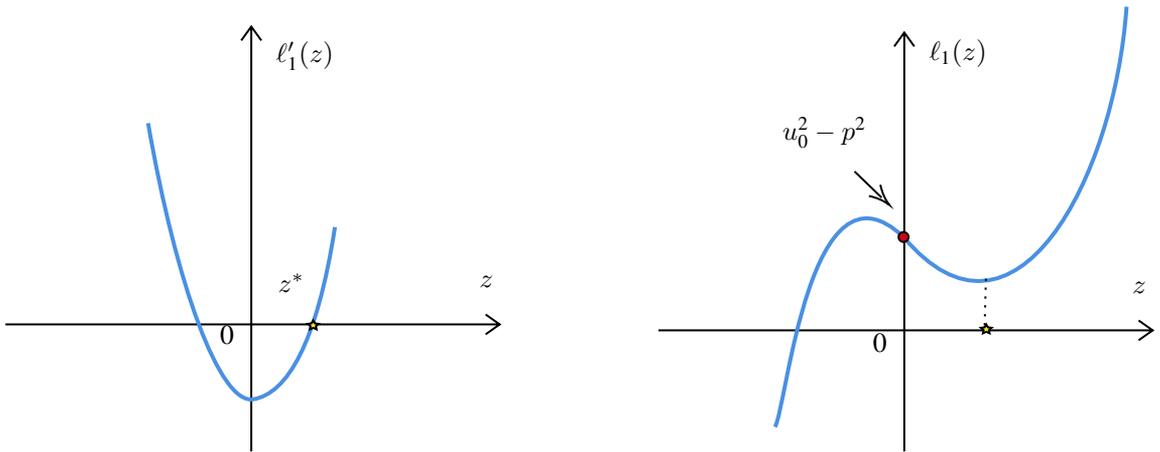


Figure 13: $u_0^2 - p^2 \geq 0, \Delta_{\ell'_1} > 0, z^* > 0, \ell_1(z^*) > 0$.

means that function ℓ_1 does not have any positive root for all $z > 0$ (see Figure 13).

To prove the condition C4, we consider the given conditions $u_0^2 - p^2 \geq 0, \Delta_{\ell'_1} > 0, z^* > 0$ and $\ell_1(z^*) < 0$. The function $\ell_1(z)$ transitions from $\ell_1(0) \geq 0$ at $z = 0$ to $\ell_1(z^*) < 0$ at z^* . Since $\ell_1(z)$ is increasing on $[0, z^*)$, it must cross the x -axis at least once in this interval, ensuring the existence of a positive root $z_r \in (0, z^*)$. For $z > z^*$, $\ell_1(z)$ is decreasing and remains negative, implying no additional positive roots exist. Hence, $\ell_1(z)$ has exactly one positive root (Figure 14).

The last condition C5 can be proven using the intermediate value theorem. If $u_0^2 - p^2 < 0$ and

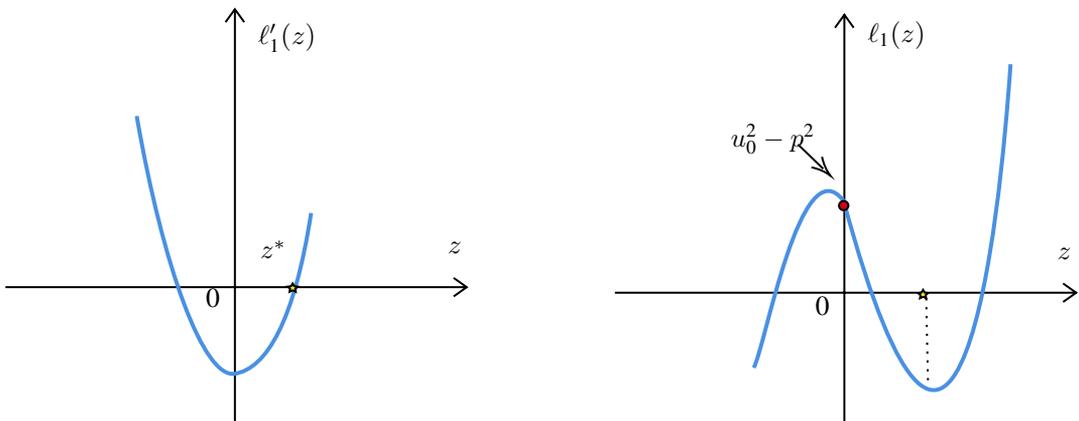


Figure 14: $u_0^2 - p^2 \geq 0, \Delta_{\ell'_1} > 0, z^* > 0, \ell_1(z^*) < 0$.

$\lim_{z \rightarrow +\infty} \ell_1(z) = +\infty$, then the condition is satisfied (see Figure 15).

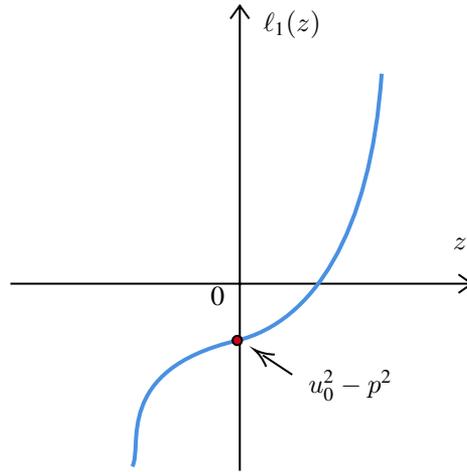


Figure 15: $u_0^2 - p^2 \leq 0$.

□

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