

Stability Analysis and Adaptive Control of Spreading Tuberculosis Disease

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Abstract

Tuberculosis disease is a widespread disease that spreads in the air from one person to another. Moreover, this contagious disease can cause damage in the lung, brain, kidney, intestine, bone and skin. Furthermore, this disease can be also latent and reactivated. For these reasons, the control analysis of this disease has a significant importance for helping its epidemic prevention. In this paper, we discuss the stability analysis of a fixed point and present a model for adaptive

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control against spreading tuberculosis disease. The stability analysis shows that the two fixed points of the tuberculosis disease are asymptotically stable. In addition, we present sufficient control conditions derived for the existence of stable tuberculosis disease.

1 Introduction

Viruses, bacteria, fungi and parasites are pathogenic microorganisms that cause infectious diseases. Such diseases can spread to others directly or indirectly from one person to another or from animals to humans and can result in deaths.

Tuberculosis, caused by the *Mycobacterium tuberculosis* bacterium, can become easily infectious and causes damage not only to the lungs but also to other organs like the brain, kidney, intestine, bone and skin [14, 23]. The World Health Organization report [25] reveals that approximately a third of the world's population is infected with tuberculosis, with millions of deaths every year.

Mathematical models have shown significant importance in analyzing the dispersion and manipulation of an infectious disease [11]. The main objective of mathematical models, is to try to understand how a given disease spreads in the population and try to take it out in the future [21]. The consequences from mathematical models can assist in determining the possibility of epidemiologic explanations and predict the impact of changes on the system dynamics. It is substantial for clarifying the population transmission dynamics of the infectious agents and the potential impact of infectious disease control programs [1,11]. Several mathematical models on tuberculosis have been developed [15,16] which have a significant role controlling tuberculosis worldwide [15]. Most of tuberculosis models we find in the literature are the SIR [12,15] or SEIR model [3,5,7,8,15,18,19]. There are clusters (or class of individuals) each of which has a status that characterizes it as responsive, inseparable, infectious or recuperative [15].

At the present time, several optimal control methods for tuberculosis disease and other diseases have been analyzed and executed [4,22]. The optimal control method performs based on minimizing the cost function defined for the problem and the limiting factors and eventually determines the control inputs of the system to achieve the specified objective. The target factors or parameters defined in the cost function can be the time of action, state error [13], control effort [24], energy consumption [9] and so on. Athithan and Ghosh [2] considered a model for tuberculosis and used a detection strat-

egy to reduce the transmission of tuberculosis in a proposed optimal control strategy and used a model with 4 groups: susceptible, exposed, infectious and recovered. Denysiuk et al. [6] considered a model for TB-HIV/AIDS by proposing an optimal control problem for it where the objective is minimization of the number of HIV-infected individuals involved with prevention and treatment of disease. The optimal control approach is utilized for systems with known parameters which obtains the system inputs with the goal of minimizing the cost function. But if variable or unsteady parameters occur in a system, then the desired results by conventional control methods may not be possible. On the other hand, we can modernize the estimation of system parameters and assure the closed-loop stability of that system by using the adaptive control method [20,22].

In this paper, we study the characteristics of the model, fixed point and Basic Reproduction Ratio [23]. Then, we present the stability analysis of a fixed point, and we design the adaptive control for stabilizing the global tuberculosis disease. Finally, we present a conclusion.

2 Preliminaries

Consider a dynamical system which satisfies

$$\dot{x} = f(x, t), x(t_0) = x_0; x \in R^n, \quad (2.1)$$

where $f(x, t) : R^n \times R^+ \rightarrow R^n$ is continuous. A point $x_e \in R^n$ is a fixed point of the system if $f(x_e, t) = 0$.

Definition 2.1. *The fixed point x_e is stable if for $\epsilon > 0$, there exists $\delta > 0$ such that*

$$\|x(0) - x_e\| < \delta \implies \|x(t) - x_e\| < \epsilon,$$

where $x(0)$ is a unique solution. *The fixed point x_e is unstable if it is not stable. The fixed point x_e is asymptotically stable if it is stable and there exists $\delta > 0$ such that*

$$\|x(0) - x_e\| < \delta \implies x(t) \rightarrow x_e \text{ as } t \rightarrow \infty.$$

The fixed point x_e is globally asymptotically stable if it is stable and

$$x(t) \rightarrow x_e \text{ as } t \rightarrow \infty.$$

The following is a fundamental result of a Lyapunov stability theorem [10].

Theorem 2.2. (*Lyapunov global asymptotically stability theorem-G.A.S*)

Suppose there is a function $V : R^n \rightarrow R$ such that

1. V is positive definite,
2. $\dot{V}(x) < 0$ for all $x \neq 0$, $\dot{V}(0) = 0$.

Then trajectories of $\dot{x} = f(x)$ converges to zero as $t \rightarrow \infty$; that is, the system is globally asymptotically stable.

Theorem 2.3. (*Lasalle's theorem[17]*)

Lasalle's theorem allows us to conclude G.A.S. of a system with only $\dot{V} \leq 0$, along with an observability type condition. We consider $\dot{x} = f(x)$. Suppose there is a function $V : R^n \rightarrow R$ such that

1. V is positive definite,
2. $\dot{V} \leq 0$,
3. the only solution of $\dot{\omega} = f(\omega)$, $\dot{V}(\omega) = 0$ is $\omega(t) = 0$. for all t .

Then the system $\dot{x} = f(x)$ is globally asymptotically stable.

Next, we consider a nonlinear nonautonomous differential equation of the general form;

$$\begin{aligned} \dot{x}(t) &= f(t, x(t)); t \geq t_0 \in R, \\ x(t_0) &= x_0 \end{aligned} \tag{2.2}$$

where the state $x(t)$ takes values in X , $f(t, x) : R \times X \rightarrow X$ is a given nonlinear function and $f(t, 0) = 0$, for all $t \in R$.

An adaptive control is an active field in the design of control systems to deal with uncertainties. To design control laws that stabilize a chaotic system, the control system can be written as equation (2.3):

$$\dot{x}(t) = f(t, x(t), u(t)); t \geq 0, \tag{2.3}$$

where $u(t)$ is the external control input.

Definition 2.4. The control system (2.3) is stabilizable if there exists the control $u(t) = k(x(t))$ such that the system

$$\dot{x}(t) = f(t, x(t), k(x(t))); t \geq 0 \tag{2.4}$$

is asymptotically stable.

3 Model Description

In this section, we study a general SIR model for the spreading of Tuberculosis disease [23]. We separate the total population $N(t)$ into three distinct subgroups: susceptible $S(t)$, infected $I(t)$, and recovered $R(t)$. A group of susceptible individuals $S(t)$ increases because of the birth π , but $S(t)$ decreases because of the death μ and the direct contact with infected individual groups β . A group of individuals that infects the tuberculosis disease $I(t)$ increases related to the rate β but decreases because of the natural mortality μ , the mortality μ_t due to tuberculosis and the rate γ . A group of recovered individuals $R(t)$ increases because of the recovery rate γ and decreases because of natural mortality μ .

Based on the assumptions, the mathematical model for spreading of tuberculosis can be represented by the following system of differential equations

$$\begin{aligned}\dot{S}(t) &= \pi - \beta SI - \mu S \\ \dot{I}(t) &= \beta SI - (\mu + \mu_t + \gamma)I \\ \dot{R}(t) &= \gamma I - \mu R,\end{aligned}\tag{3.5}$$

with $N(t) = S(t) + I(t) + R(t)$ and the initial condition

$$S(0) \geq 0, I(0) \geq 0, R(0) \geq 0$$

By considering the total population density, we have $S(t) + I(t) + R(t) = 1$. So $R(t) = 1 - S(t) - I(t)$. Therefore, it is enough to consider

$$\begin{aligned}\dot{S}(t) &= \pi - \beta SI - \mu S \\ \dot{I}(t) &= \beta SI - (\mu + \mu_t + \gamma)I\end{aligned}\tag{3.6}$$

such that the region for the above system is written as

$$\Omega = \{(S(t), I(t)) \in R_+^2, S(t) + I(t) \leq 1\}$$

4 Mathematical Analysis

4.1 Fixed Point and Basic Reproduction Ratio

In this section, we study the fixed point and the basic reproduction ratio R_0 of the tuberculosis disease model [23]. The fixed point was obtained when we set the right hand side of the system (3.6) equal to zero or $\dot{S}(t) = 0$ and

$\dot{I}(t) = 0$. Thus the two fixed points are obtained as follows [23]:

1. The first fixed point is $E_0(S_0, I_0) = (\frac{\pi}{\mu}, 0)$. This is the disease free fixed point.

2. The second fixed point is $E_1(S_1, I_1) = (\frac{\mu+\mu_t+\gamma}{\beta}, \frac{\pi}{\mu+\mu_t+\gamma} - \frac{\mu}{\beta})$. This is the epidemic or infection occurred.

To handle infection, the following must be satisfied $S_1 \geq \frac{\pi}{\mu}$, where $S_1 = \frac{\mu+\mu_t+\gamma}{\beta}$. We conclude that

1. If $\frac{\mu+\mu_t+\gamma}{\beta} \geq \frac{\pi}{\mu}$, then an epidemic will not occur or the disease will not be transmitted. 2. If $\frac{\mu+\mu_t+\gamma}{\beta} < \frac{\pi}{\mu}$, then there will be an epidemic or an infection occurrence.

Next, the basic reproduction ratio R_0 can be found in [23]. If the disease is not transmitted, then $S_1 \geq \frac{\pi}{\mu}$ or $\frac{\pi}{\mu S_1} \leq 1$, or $\frac{\beta\pi}{\mu(\mu+\mu_t+\gamma)} - 1 \leq 0$ in order to obtain the basic reproduction ratio $R_0 = \frac{\beta\pi}{\mu(\mu+\mu_t+\gamma)}$ which can be used to measure the rate of spreading of the disease.

1. For $R_0 \leq 1$, the disease will disappear.
2. For $R_0 > 1$, the disease will be epidemic.

4.2 Stability Analysis of Fixed Point

In this section, we discuss the stability analysis of both fixed points. We use Lasalle's Theorem for both of the fixed points of the proposed model, the disease free fixed point and the epidemic fixed point. First, we give the globally asymptotically stability of the disease free fixed point.

Theorem 4.1. *If $R_0 \leq 1$, then the disease free fixed point $E_0(S_0, I_0) = (\frac{\pi}{\mu}, 0)$ of the system is globally asymptotically stable on Ω .*

Proof. To establish the globally asymptotically stability of the disease free fixed point E_0 , we construct the Lyapunov function V . Let $V : \Omega \rightarrow R$, be defined by

$$V(S, I) = I(t).$$

Considering the time derivative of V along the solution of the system, we obtain

$$\begin{aligned} \dot{V}(t) &= \beta SI - (\mu + \mu_t + \gamma)I \\ &= (\mu + \mu_t + \gamma) \left[\frac{\beta SI}{\mu + \mu_t + \gamma} - I \right] \\ &= (\mu + \mu_t + \gamma) \left[\frac{\beta \pi}{\mu(\mu + \mu_t + \gamma)} - 1 \right] I \\ &= (\mu + \mu_t + \gamma)(R_0 - 1)I, \end{aligned}$$

where R_0 is the basic reproduction ratio. We see that $\dot{V}(t) \leq 0$ for $R_0 \leq 1$. Therefore, by the Lasalle's Theorem [17], the disease free fixed point E_0 of the system is globally asymptotically stable on Ω .

Theorem 4.2. *The epidemic fixed point $E_1(S_1, I_1) = (\frac{\mu + \mu_t + \gamma}{\beta}, \frac{\pi}{\mu + \mu_t + \gamma} - \frac{\mu}{\beta})$ of the system is globally asymptotically stable on Ω .*

Proof. To establish the globally asymptotically stability of the epidemic fixed point $E_1 = (S^*, I^*)$, where $S^* = \frac{\mu + \mu_t + \gamma}{\beta}$ and $I^* = \frac{\pi}{\mu + \mu_t + \gamma} - \frac{\mu}{\beta}$, we construct the Lyapunov function $V : \Omega_+ \rightarrow R$, where

$$\Omega_+ = \{(S(t), I(t)) \in \Omega \mid S(t) > 0, I(t) > 0\}$$

is given by

$$V(S, I) = V_1[S - S^* \ln(\frac{S}{S^*})] + V_2[I - I^* \ln(\frac{I}{I^*})],$$

where V_1 and V_2 are positive constants to be chosen. By taking the derivative of the above function, we obtain

$$\begin{aligned} \dot{V} &= [V_1 S - V_1 S^*] \left[\frac{\pi}{S} - \beta I - \mu \right] + [V_2 I - V_2 I^*] [\beta S - (\mu + \mu_t + \gamma)] \\ &= V_1 [S - S^*] \left[\frac{\pi}{S} - \beta I - \mu \right] + V_2 [I - I^*] [\beta S - (\mu + \mu_t + \gamma)] \end{aligned}$$

Considering the fixed point, we have

$$-\mu = \beta I^* - \frac{\pi}{S^*} \text{ and } -(\mu + \mu_t + \gamma) = -\beta S^*$$

Hence, the above equation becomes

$$\begin{aligned}
\dot{V} &= V_1[S - S^*]\pi\left[\frac{S^* - S}{SS^*}\right] - V_1(S - S^*)\beta(I - I^*) + V_2(I - I^*)\beta(S - S^*) \\
&= -V_1[S - S^*]\pi\left[\frac{S - S^*}{SS^*}\right] - V_1(S - S^*)\beta(I - I^*) + V_2(I - I^*)\beta(S - S^*) \\
&= -V_1\pi\frac{(S - S^*)^2}{SS^*} + \beta(V_2 - V_1)(S - S^*)(I - I^*) \\
&= \beta(V_2 - V_1)(S - S^*)(I - I^*) - V_1\pi\frac{(S - S^*)^2}{SS^*}.
\end{aligned}$$

For $V_1 = V_2 = 1$, we have

$$\dot{V} = -\pi\frac{(S - S^*)^2}{SS^*} \leq 0.$$

We also obtain

$$\dot{V} = 0 \iff S = S^*$$

Therefore, by the Lasalle's Theorem [17], the epidemic fixed point E_1 of the system is globally asymptotically stable on Ω .

4.3 Adaptive Control of Tuberculosis Disease

In this section, we design the adaptive control for the global stabilized tuberculosis disease. The sufficient control conditions are derived by using Lyapunov stability theorem.

Theorem 4.3. *The tuberculosis disease is global stabilized for the initial conditions $S(t) > 0, I(t) > 0, R(t) > 0$ by the adaptive control u_1, u_2 , where the estimate parameters are given by $\hat{\pi} = S + K_3e_\pi, \hat{\beta} = SI^2 + K_4e_\beta, \hat{\mu} = -S^2 + K_5e_\mu, \hat{\mu}_t = -I^2 + K_6e_{\mu_t}$, and $\hat{\gamma} = -I^2 + K_7e_\gamma$.*

Proof. We design the adaptive control for the tuberculosis disease as follows:

$$\begin{aligned}
\dot{S}(t) &= \pi - \beta SI - \mu S + u_1 \\
\dot{I}(t) &= \beta SI - (\mu + \mu_t + \gamma)I + u_2,
\end{aligned} \tag{4.7}$$

where u_1 and u_2 are controllers to be designed by using the states and estimates of the parameters of the system. We consider the adaptive control

functions

$$\begin{aligned} u_1 &= -\hat{\pi} + \hat{\beta}SI + \hat{\mu}S - k_1S \\ u_2 &= -\hat{\beta}SI + (\hat{\mu} + \hat{\mu}_t + \hat{\gamma})I - k_2I, \end{aligned} \quad (4.8)$$

where $\hat{\pi}$, $\hat{\beta}$, $\hat{\mu}$, $\hat{\mu}_t$, and $\hat{\gamma}$ are estimates of the parameters and k_1 and k_2 are positive constants. Substituting the controllers, we have

$$\begin{aligned} \dot{S}(t) &= (\pi - \hat{\pi}) - (\beta - \hat{\beta})SI - (\mu - \hat{\mu})S - k_1S \\ \dot{I}(t) &= (\beta - \hat{\beta})SI - (\mu - \hat{\mu})I - (\mu_t - \hat{\mu}_t)I - (\gamma - \hat{\gamma})I - k_2I. \end{aligned} \quad (4.9)$$

Define the parameter errors as

$$e_\pi = \pi - \hat{\pi}, e_\beta = \beta - \hat{\beta}, e_\mu = \mu - \hat{\mu}, e_{\mu_t} = \mu_t - \hat{\mu}_t, e_\gamma = \gamma - \hat{\gamma}. \quad (4.10)$$

Thus, equation (4.9) can be rewritten as

$$\begin{aligned} \dot{S}(t) &= e_\pi - e_\beta SI - e_\mu S - k_1S \\ \dot{I}(t) &= e_\beta SI - e_\mu I - e_{\mu_t} I - e_\gamma I - k_2I \end{aligned} \quad (4.11)$$

Consider the quadratic Lyapunov function

$$V = \frac{1}{2}(S^2 + I^2 + e_\pi^2 + e_\beta^2 + e_\mu^2 + e_{\mu_t}^2 + e_\gamma^2), \quad (4.12)$$

which is a positive definite function on R^7 . So

$$\dot{e}_\pi = -\dot{\hat{\pi}}, \dot{e}_\beta = -\dot{\hat{\beta}}, \dot{e}_\mu = -\dot{\hat{\mu}}, \dot{e}_{\mu_t} = -\dot{\hat{\mu}}_t, \dot{e}_\gamma = -\dot{\hat{\gamma}}. \quad (4.13)$$

Differentiating V in equation (4.11) and using equation (4.13), we get

$$\begin{aligned} \dot{V}(t) &= Se_\pi - e_\beta S^2 I - e_\mu S^2 - k_1 S^2 + e_\beta SI^2 - e_\mu I^2 - e_{\mu_t} I^2 \\ &\quad - e_\gamma I^2 - k_2 I^2 - e_\pi \dot{\hat{\pi}} - e_\beta \dot{\hat{\beta}} - e_\mu \dot{\hat{\mu}} - e_{\mu_t} \dot{\hat{\mu}}_t - e_\gamma \dot{\hat{\gamma}}. \end{aligned} \quad (4.14)$$

The estimated parameters of equation (4.14) are updated by the following

$$\begin{aligned} \dot{\hat{\pi}} &= S + k_3 e_\pi \\ \dot{\hat{\beta}} &= SI^2 + k_4 e_\beta \\ \dot{\hat{\mu}} &= -S^2 + k_5 e_\mu \\ \dot{\hat{\mu}}_t &= -I^2 + k_6 e_{\mu_t} \\ \dot{\hat{\gamma}} &= -I^2 + k_7 e_\gamma, \end{aligned} \quad (4.15)$$

where k_3, k_4, k_5, k_6, k_7 are positive constants. Substituting equation (4.15) into equation (4.14), we obtain

$$\dot{V}(t) = -e_\beta S^2 I - e_\mu I^2 - k_1 S^2 - k_2 I^2 - k_3 e_\pi^2 - k_4 e_\beta^2 - k_5 e_\mu^2 - k_6 e_{\mu t}^2 - k_7 e_\gamma^2$$

which is a negative definite function on R^7 . Therefore, by Lyapunov stability theorem [10], We obtain that the tuberculosis disease is global stabilized for the initial conditions $S(t) > 0, I(t) > 0, R(t) > 0$ by the adaptive control u_1, u_2 , where the estimate parameters are given by $\hat{\pi} = S + K_3 e_\pi, \hat{\beta} = SI^2 + K_4 e_\beta, \hat{\mu} = -S^2 + K_5 e_\mu, \hat{\mu}_t = -I^2 + K_6 e_{\mu t}$, and $\hat{\gamma} = -I^2 + K_7 e_\gamma$.

5 Conclusions

In this paper, we studied a model of Tuberculosis disease, the fixed points and the reproduction ratio R_0 . We analyzed the stability of fixed points and found the adaptive control of Tuberculosis disease. The mathematical analysis of the model showed that there are two fixed points, one is the disease free fixed point and the other is the epidemic fixed point. The proposed model was determined by the basic reproduction ratio R_0 which depends on the parameter values. Analyzing the stability of fixed points showed that the disease free fixed point of the system is globally asymptotically stable when $R_0 \leq 1$ and the epidemic fixed point of the system is globally asymptotically stable. Moreover, the tuberculosis disease is global stabilized for the initial conditions $S(t) > 0, I(t) > 0, R(t) > 0$ by using the obtained adaptive control and the parameter estimates.

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