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ANALYSIS OF A FRACTIONAL ORDER MATHEMATICAL MODEL FOR TUBERCULOSIS WITH OPTIMAL CONTROL

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Abstract. In this paper, a fractional-order mathematical model with control is constructed to describe the transmission of tuberculosis. Two cases are considered: the constant control and the optimal control. In the former case, the stability conditions of the disease-free equilibrium and the endemic equilibrium are obtained. In the second case, optimal control theory is applied to the corresponding model. The optimal control formula is derived by use of the Hamiltonian function and the Pontryagin's Maximum Principle. In addition, some numerical simulations are performed to support our analytic results.

Keywords. Fractional order; Tuberculosis; Basic reproduction number; Stability; Optimal control.

1. INTRODUCTION

Tuberculosis is an infectious respiratory disease caused by mycobacterium tuberculosis. Despite advances in technology, tuberculosis (TB) remains one of the world top 10 causes of death. Recent data suggest that the global incidence of TB is rising, and this is mainly because of its association with the human immunodeficiency virus (HIV) [1]. In 2017, 10 million people were infected with TB, and 1.6 million died from the disease (including 0.3 million with HIV). Ending the TB epidemic by 2030 is among the health targets of the Sustainable Development Goals [2].

The human immune response limits the proliferation of bacteria after the initial infection. As a result, most infected people remain latent throughout their lives, with about 10% of those infected eventually developing active TB. The average incubation period (non-infectious) for TB can range from a few months to several decades [3]. Because of treatment and prevention methods are so different, it is critical to accurately classify the TB situation. Tuberculosis, of course, can be treated with drugs [4]. But most high-incidence patients also use only existing TB vaccines, Calmette-Guérin. And its effectiveness in preventing TB is controversial [5]. In recent years, treatment has become difficult due to the emergence of drug-resistant strains of

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Mtb [6, 7]. The cure rate of ordinary tuberculosis patient is more than 90%. However, the cure rate of multidrug resistant tuberculosis patient is only about 50%, and the treatment cycle is as long as 18-24 months [2]. So, in addition to controlling TB in terms of treatment, it needs to be controlled in other ways.

Recently, the theoretical analysis of fractional differential equations and the study of numerical methods have become the focus of people's attention. Fractional calculus is a method to extend the classical integral order calculus to real or complex order [8, 9, 10, 11, 12]. Fractional derivative is a good mathematical tool to describe the memory and genetic characteristics of complex systems [13]. At present, there are more than six definitions of fractional derivative, among which Riemann-Liouville and Caputo derivatives are the most commonly used [14]. As we all know, in the case of time fractional Caputo derivative, the initial conditions are expressed by the values of the unknown function and its integer derivative with clear physical meaning [15]. So, we will adapt the Caputo's definition in our paper. In recent years, fractional differential equations also have been widely used in physics, chemistry, electricity, biology, economics, epidemiology and other fields [16, 17, 18, 19, 20].

It is known that mathematical models play a crucial role in many dynamics and control, including epidemics of malaria and tuberculosis [21, 22, 23, 24, 25]. Moreover, the enormous public health burden of TB requires the use of mathematical models to understand the dynamics of transmission and to identify effective control strategies. Particularly, in [26], Sweilam and Mekhlafi studied optimal control for fractional general nonlinear multi-strain tuberculosis model. The results show that the fractional-order model can describe more complex dynamical processes than the integer model, and can easily include memory effects that exist in the real world. In recent years, more and more scholars studied the optimal control of fractional order, for example [27, 28, 29, 30]. The aim of this paper is to investigate the best control methods to minimize the number of active, infectious and latent TB patients, taking into account the cost of treating TB patients.

Recently, Liu and Zhang [31] investigated the following tuberculosis model:

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - \beta S(I+\rho_1 T) - (\mu+p)S, \\ \dfrac{\mathrm{d}V}{\mathrm{d}t} = pS - \rho_2\beta V(I+\rho_1 T) - \mu V, \\ \dfrac{\mathrm{d}L}{\mathrm{d}t} = l\beta S(I+\rho_1 T) + \rho_2\beta V(I+\rho_1 T) - (\mu+\delta)L + \rho T, \\ \dfrac{\mathrm{d}I}{\mathrm{d}t} = (1-l)\beta S(I+\rho_1 T) + \delta L - (\mu+\varepsilon+\gamma)I, \\ \dfrac{\mathrm{d}T}{\mathrm{d}t} = \gamma I - (\mu+\rho)T, \\ N(t) = S(t)+V(t)+L(t)+I(t)+T(t). \end{cases} \tag{1.1}$$

In the model above, the incidence rate was bilinear. Incidence is a very important factor in infectious disease models, the most commonly used contact rate are bilinear incidence and standard incidence. Between these two contact rates, there is a more realistic saturation contact rate [32, 33]. Because it contains behavioral changes and population effects of infected individuals, the unbounded exposure rate can be prevented by selecting appropriate parameters. Saturation rates were used in many epidemic models; see, for example, [34, 35].

Thus, based on the integer order tuberculosis model (1.1), we put forward an improved fractional order tuberculosis infection model with saturating incidence rate as follows:

$$\begin{cases} D^{\alpha}S(t) = \Lambda - \dfrac{\beta SI}{1+\theta_1 I} - \rho_1\beta ST - (\mu+p)S, \\ D^{\alpha}V(t) = pS - \dfrac{\rho_2\beta VI}{1+\theta_2 I} - \rho_1\rho_2\beta VT - \mu V, \\ D^{\alpha}L(t) = \dfrac{l\beta SI}{1+\theta_1 I} + \rho_1 l\beta ST + \dfrac{\rho_2\beta VI}{1+\theta_2 I} + \rho_1\rho_2\beta VT - (\mu+\delta)L + \rho T, \\ D^{\alpha}I(t) = \dfrac{(1-l)\beta SI}{1+\theta_1 I} + (1-l)\rho_1\beta ST + \delta L - (\mu+\varepsilon+\gamma)I, \\ D^{\alpha}T(t) = \gamma I - (\mu+\rho)T, \end{cases} \tag{1.2}$$

where $\rho_1 < 1$, and $\rho_2 < 1$. Obviously, the biologically feasible region of the above system (1.2) is

$$\Omega = \left\{ (S,\, V,\, L,\, I,\, T) \in R_+^5 : S \le \frac{\Lambda}{\mu+p},\, V \le \frac{\Lambda p}{\mu(\mu+p)},\, N \le \frac{\Lambda}{\mu} \right\}.$$

In Eq. (1.2) D^{α} $(0 < \alpha < 1)$ denotes Caputo fractional differential operator, and the model are based on the following scenarios:

(H1) $S(t)$, $V(t)$, $L(t)$, $I(t)$ and $T(t)$ represent susceptible population, vaccinated population, population infected with TB in latent (asymptomatic) stage, population infected with TB in the active stage and treated population infected with TB, respectively.

(H2) We assumed that vaccinated individuals could also be infected.

(H3) We assumed that that treated individuals also had the ability to infect others during treatment.

(H4) Due to drug resistance, reinfection may also occur after treatment and enter the incubation period.

The descriptions of parameters are listed in Table 1, and some parameter values are take from [36, 37, 38].

TABLE 1. Description of the parameters for system (1.2)

Parameters	Description	Default value
Λ	the recruitment of the susceptible class	1428 person year^{-1}
β	the disease transmission coefficient	(0, 1)
ρ_1	the infectiousness among individuals with active TB who are treated	0.25
ρ_2	the reduction in risk of infection due to vaccination	(0, 1)
μ	the natural death rate	0.014 year^{-1}
l	susceptible individuals who acquire infection and move to latent TB class	(0, 1)
δ	the rate of individuals leave class L for class I	(0, 1)
ε	the death rate due to disease	(0.1, 1)
p	the vaccination rate	(0, 1)
ρ	the rate of successfully treated individuals and return to latent TB class	(0.1, 1)
γ	the rate of infectious individuals who are treated	(0, 1)
$\theta_1,\ \theta_2$	half-saturation constant	(0,1)

The paper is organized as follows. In Section 2, we introduce some definitions and lemmas for fractional-order differential equations. In Section 3, we study the existence and stability

of equilibrium points and numerical simulations. In Section 4, we present the formulation of the optimal control problems and investigate the existence of an optimal control function and derive an optimal system characterizing the optimal control and numerical simulations. In the last section, Section 5, some conclusions and discussions are provided.

2. PRELIMINARIES

For convenience, we list some of the basic definitions and lemmas of the fractional calculus. In fractional-order calculus, there are many fractional-order integration and fractional-order differentiation that have been defined, for example, the Grunwald-Letnikov (GL) definition, the Riemann-Liouville (RL) definition and the Caputo definition. Since the initial condition is the same as the form of integral differential equation, we will adopt the definition of Caputo in this paper.

Definition 2.1. [15] The Riemann-Liouville fractional integral of order $\alpha > 0$ for a function $f : R^+ \to R$ is defined by

$$ {}_0D_t^{-\alpha} f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} f(s) \mathrm{d}s, \ t \geq 0. $$

Based on this definition of Riemann-Liouville fractional integral, the fractional-order derivative in Riemann-Liouville sense and Caputo sense are given below.

Definition 2.2. [15] The Riemann-Liouville fractional derivative of order $\alpha > 0$ for a function $f : R^+ \to R$ is defined by

$$ {}_0^{RL}D_t^{\alpha} f(t) = \frac{\mathrm{d}^k}{\mathrm{d}t^k} ({}_0D_t^{-(k-\alpha)} f(t)) = \frac{1}{\Gamma(k-\alpha)} \frac{\mathrm{d}^k}{\mathrm{d}t^k} \int_0^t (t-s)^{k-\alpha-1} f(s) \mathrm{d}s, \ t \geq 0, $$

where $k-1 \leq \alpha < k, \ k \in N$ and $\Gamma(\cdot)$ is the Gamma function, that is,

$$ \Gamma(\alpha) = \int_0^{+\infty} t^{\alpha-1} e^{-t} \mathrm{d}t. $$

In particular, if $0 < \alpha < 1$, then

$$ {}_0^{RL}D_t^{\alpha} f(t) = \frac{1}{\Gamma(1-\alpha)} \frac{\mathrm{d}}{\mathrm{d}t} \int_0^t (t-s)^{-\alpha} f(s) \mathrm{d}s. $$

Definition 2.3. [15] The Caputo fractional derivative of order $\alpha > 0$ for a function $f : R^+ \to R$ is defined by

$$ {}_0^{C}D_t^{-\alpha} f(t) = {}_0 D_t^{-(k-\alpha)} f^{(k)}(t) = \frac{1}{\Gamma(k-\alpha)} \int_0^t (t-s)^{k-\alpha-1} f^{(k)}(s) \mathrm{d}s, \quad t \geq 0, $$

where $k-1 \leq \alpha < k, \ k \in N$ and $f^{(m)}(t)$ is the m-order derivative of f(t). In particular, if $0 < \alpha < 1$, then

$$ {}_0^{C}D_t^{-\alpha} f(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{f^{'}(s)}{(t-s)^{\alpha}} \mathrm{d}s. $$

Theorem 2.4. [39] *Consider the following commensurate fractional-order system:*

$$ \frac{\mathrm{d}^{\alpha} x}{\mathrm{d}t^{\alpha}} = f(x), \quad x(0) = x_0, $$

with $0<\alpha<1$ *and* $x\in R^n$. *The equilibrium points of the above system are calculated by solving the equation:* $f(x)=0$. *These points are locally asymptotically stable if all eigenvalues* λ_i *of the Jacobian matrix evaluated at the equilibrium points satisfy the inequality:* $|\arg(\lambda_i)|>\dfrac{\alpha\pi}{2}$.

3. Qualitative analysis of system (1.2)

3.1. **The reproduction number and the existence of equilibriums.** The basic reproduction number R_0 means that the expected number of new infections generated by a single infected person during his/her entire period of infectiousness when introduced in a completely susceptible population, which can be derived by using the next generation operator technique [40, 41]. From this method, we get the basic reproduction number of system (1.2) as follows

$$R_0=\rho(FV^{-1})=\frac{\beta(\mu+\rho+\gamma\rho_1)(\delta\rho_2V^0+\delta S^0+\mu(1-l)S^0)}{(\mu+\delta)(\mu+\rho)(\mu+\varepsilon)+(\mu+\delta+\rho)\mu\gamma},$$

where $\rho(\cdot)$ represents the spectral radius. The matrixes F, and V are given by

$$F=\begin{pmatrix}0 & \beta(lS^0+\rho_2V^0) & \rho_1\beta(lS^0+\rho_2V^0)\\ 0 & (1-l)\beta S^0 & (1-l)\rho_1\beta S^0\\ 0 & 0 & 0\end{pmatrix},\qquad V=\begin{pmatrix}\mu+\delta & 0 & -\rho\\ -\delta & b_2 & \mu+\varepsilon+\gamma\\ 0 & -\gamma & \mu+\rho\end{pmatrix},$$

where $S^0=\dfrac{\Lambda}{\mu+p}$, and $V^0=\dfrac{\Lambda p}{\mu(\mu+p)}$.

The equilibriums of model (1.2) are obtained by solving the algebraic system

$$\begin{cases}\Lambda-\dfrac{\beta SI}{1+\theta_1I}-\rho_1\beta ST-(\mu+p)S=0,\\ pS-\dfrac{\rho_2\beta VI}{1+\theta_2I}-\rho_1\rho_2\beta VT-\mu V=0,\\ \dfrac{l\beta SI}{1+\theta_1I}+\rho_1l\beta ST+\dfrac{\rho_2\beta VI}{1+\theta_2I}+\rho_1\rho_2\beta VT-(\mu+\delta)L+\rho T=0,\\ \dfrac{(1-l)\beta SI}{1+\theta_1I}+(1-l)\rho_1\beta ST+\delta L-(\mu+\varepsilon+\gamma)I=0,\\ \gamma I-(\mu+\rho)T=0.\end{cases}$$

By simple calculation, we obtain two equilibriums of system (1.2), namely,

(1) disease-free equilibrium $E_0=\left(S^0,\,V^0,\,0,\,0,\,0\right)$;

(2) endemic equilibrium $E^*=(S^*,\,V^*,\,L^*,\,I^*,\,T^*)$, where

$$S^*=\frac{\Lambda(1+\theta_1I^*)}{\beta I^*+(1+\theta_1I^*)(\rho_1\beta\frac{\gamma}{\mu+\rho}I^*+\mu+p)},\qquad V^*=\frac{pS^*(1+\theta_2I^*)}{\rho_2\beta I^*+(1+\theta_2I^*)(\rho_1\rho_2\beta T^*+\mu)},$$

$$L^*=\frac{1}{\mu+\delta}\left(\frac{l\beta S^*I^*}{1+\theta_1I^*}+\rho_1l\beta S^*T^*+\frac{\rho_2\beta V^*I^*}{1+\theta_2I^*}+\rho_1\rho_2\beta V^*T^*+\rho T^*\right),\quad T^*=\frac{\gamma}{\mu+\rho}I^*,$$

and I^* is determined by the following equation

$$A_1I^4+A_2I^3+A_3I^2+A_4I+A_5=0,\tag{3.1}$$

where

$$
\begin{aligned}
A_1 &= \theta_1\theta_2\rho_1^2\rho_2\beta^2\left(\frac{\gamma}{\mu+\rho}\right)^2\frac{1}{\mu(\mu+p)}>0,\\
A_2 &= -\frac{\theta_1\theta_2\rho_1^2\rho_2\beta^2\gamma^2\Lambda[\mu(1-l)+\delta]}{\mu(\mu+p)(\mu+\rho)[(\mu+\delta)(\mu+\rho)(\mu+\varepsilon)+(\mu+\delta+\rho)\mu\gamma]}\\
&\quad -\frac{\rho_1\beta\gamma\theta_1}{\mu(\mu+p)(\mu+\rho)}\left(\rho_2\beta+\frac{\rho_1\rho_2\beta\gamma}{\mu+\rho}+\mu\theta_2\right)\\
&\quad +\frac{\rho_1\beta\gamma\rho_2\delta\theta_2}{\mu(\mu+p)(\mu+\rho)}\left[\beta+\frac{\rho_1\beta\gamma}{\mu+\rho}+\theta_1(\mu+p)\right],\\
A_3 &= -\frac{\rho_1\beta\Lambda\gamma[\mu(1-l)+\delta]\left[\rho_2\beta\theta_2\left(1+\frac{\rho_1\gamma}{\mu+\rho}\right)+\theta_1\left(\rho_2\beta+\frac{\rho_1\rho_2\beta\gamma}{\mu+\rho}+\mu\theta_2\right)\right]}{\mu(\mu+p)[(\mu+\delta)(\mu+\rho)(\mu+\varepsilon)+(\mu+\delta+\rho)\mu\gamma]]}\\
&\quad -\frac{\theta_1\theta_2\rho_1\rho_2\beta p\Lambda\gamma\delta}{\mu(\mu+p)[(\mu+\delta)(\mu+\rho)(\mu+\varepsilon)+(\mu+\delta+\rho)\mu\gamma]}\\
&\quad +\frac{1}{\mu(\mu+p)}\left[\beta+\rho_1\frac{\beta\gamma}{\mu+\rho}+\theta_1(\mu+p)\right]\left(\rho_2\beta+\rho_1\rho_2\frac{\beta\gamma}{\mu+\rho}+\mu\theta_2\right)\\
&\quad +\frac{1}{\mu(\mu+p)}\left[\mu\theta_1\rho_1\frac{\beta\gamma}{\mu+\rho}+\theta_2\rho_1\rho_2\frac{\beta\gamma}{\mu+\rho}(\mu+p)\right],\\
A_4 &= -\frac{\beta\Lambda[\mu(1-l)+\delta]\left(\rho_2\beta+\rho_1\rho_2\frac{\beta\gamma}{\mu+\rho}+\mu\theta_2\right)(\mu+\rho+\rho_1\gamma)}{\mu(\mu+p)[(\mu+\delta)(\mu+\rho)(\mu+\varepsilon)+(\mu+\delta+\rho)\mu\gamma]}\\
&\quad -\frac{\beta\Lambda\{\theta_1\mu\rho_1\gamma[\mu(1-l)+\delta]+\theta_1\rho_2p\delta(\mu+\rho)+\rho_1\rho_2p\gamma\delta(\theta_1+\theta_2)\}}{\mu(\mu+p)[(\mu+\delta)(\mu+\rho)(\mu+\varepsilon)+(\mu+\delta+\rho)\mu\gamma]]}\\
&\quad +\frac{1}{\mu(\mu+p)}\left\{\mu\left(\beta+\rho_1\frac{\beta\gamma}{\mu+\rho}+\theta_1(\mu+p)\right)+(\mu+p)\left(\rho_2\beta+\frac{\rho_1\rho_2\beta\gamma}{\mu+\rho}+\mu\theta_2\right)\right\},\\
A_5 &= 1-R_0.
\end{aligned}
$$

If $R_0>1$, then Descartes rule of sign ensures that the above Eq.(3.1) possesses at least one positive root.

3.2. **The stability of the equilibriums.** The Jacobian matrix of system (1.2) reads as

$$
J=\begin{pmatrix}
a_{11} & 0 & 0 & a_{14} & -\rho_1\beta S\\
p & a_{22} & 0 & a_{24} & -\rho_1\rho_2\beta V\\
a_{31} & a_{32} & -(\mu+\delta) & a_{34} & a_{35}\\
a_{41} & 0 & \delta & a_{44} & (1-l)\rho_1\beta S\\
0 & 0 & 0 & \gamma & -(\mu+\rho)
\end{pmatrix},
$$

where

$$
\begin{aligned}
a_{11} &= -\frac{\beta I}{1+\theta_1 I}-\rho_1\beta T-(\mu+p), & a_{14} &= -\frac{\beta S}{(1+\theta_1 I)^2},\\
a_{22} &= -\frac{\rho_2\beta I}{1+\theta_2 I}-\rho_1\rho_2\beta T-\mu, & a_{24} &= -\frac{\rho_2\beta V}{(1+\theta_2 I)^2},\\
a_{31} &= \frac{l\beta I}{1+\theta_1 I}+\rho_1 l\beta T, & a_{32} &= \frac{\rho_2\beta I}{1+\theta_2 I}+\rho_1\rho_2\beta T,\\
a_{34} &= \frac{l\beta S}{(1+\theta_1 I)^2}+\frac{\rho_2\beta V}{(1+\theta_2 I)^2}, & a_{35} &= \rho_1 l\beta S+\rho_1\rho_2\beta V+\rho,\\
a_{41} &= \frac{(1-l)\beta I}{1+\theta_1 I}+(1-l)\rho_1\beta T, & a_{44} &= \frac{(1-l)\beta S}{(1+\theta_1 I)^2}-(\mu+\varepsilon+\gamma).
\end{aligned}
$$

The Jacobian matrix of system (1.2) at equilibrium point E_0 is

$$J(E_0)=\begin{pmatrix} -(\mu+p) & 0 & 0 & -\beta S^0 & -\rho_1\beta S^0 \\ p & -\mu & 0 & -\rho_2\beta V^0 & -\rho_1\rho_2\beta V^0 \\ 0 & 0 & -(\mu+\delta) & l\beta S^0+\rho_2\beta V^0 & \rho_1(l\beta S^0+\rho_2\beta V^0)+\rho \\ 0 & 0 & \delta & (1-l)\beta S^0-(\mu+\varepsilon+\gamma) & (1-l)\rho_1\beta S^0 \\ 0 & 0 & 0 & \gamma & -(\mu+\rho) \end{pmatrix}.$$

The corresponding characteristic equation of the above matrix is

$$(\lambda+\mu+p)(\lambda+\mu)(\lambda^3+a_1\lambda^2+a_2\lambda+a_3)=0.$$

It is obvious that two eigenvalues can be directly obtained: $\lambda_1=-(\mu+p)<0$, $\lambda_2=-\mu<0$, and the other eigenvalues are determined by the following equation

$$Q(\lambda)=\lambda^3+a_1\lambda^2+a_2\lambda+a_3=0,$$

where

$$\begin{aligned} a_1 &= (\mu+\rho)+(\mu+\delta)+(\mu+\varepsilon+\gamma)-(1-l)\beta S^0, \\ a_2 &= -(2\mu+\rho+\delta)[(1-l)\beta S^0-(\mu+\varepsilon+\gamma)]-(1-l)\gamma\rho_1\beta S^0 \\ &\quad -\delta\beta(lS^0+\rho_2 V_0)+(\mu+\rho)(\mu+\delta), \\ a_3 &= 1-R_0. \end{aligned}$$

Let $D(Q)$ denote the discriminant of a polynomial $Q(\lambda)=\lambda^3+a_1\lambda^2+a_2\lambda+a_3$. From [42, Proposition 1], we get

$$D(Q)=18a_1a_2a_3+(a_1a_2)^2-4a_3a_1^3-4a_2^3-27a_3^3.$$

Then the following properties can be obtained from [42, Proposition 1].

Proposition 3.1. *The equilibrium E_0 is asymptotically stable if one of the following conditions holds for polynomial Q and $D(Q)$:*
(1)$D(Q)>0$, $a_1>0$, $a_3>0$ *and* $a_1a_2>a_3$,
(2)$D(Q)<0$, $a_1\geq 0$, $a_2\geq 0$, $a_3\geq 0$ *and* $\alpha<\frac{2}{3}$,
(3)$D(Q)<0$, $a_1>0$, $a_2>0$, $a_1a_2=a_3$ *and* $\alpha\in(0,1)$.

Next, we discuss the global asymptotic stability of the disease-free equilibrium.

Theorem 3.2. *If $R_0\leq 1$, then the disease-free equilibrium E_0 of system (1.2) is global asymptotically stable within Ω.*

Proof. Consider the following Lyapunov function

$$V=\delta L+(\mu+\delta)I+AT,$$

where $A = \dfrac{\delta\rho_1 l\beta S^0 + \rho_1\rho_2\beta V^0 + \rho + (\mu+\delta)(1-l)\rho_1\beta S^0}{\mu+\rho}$. Then,

$$\begin{aligned}
& D_t^\alpha V|_{(1.2)} \\
= \;& \delta\left[\frac{l\beta SI}{1+\theta_1 I} + \rho_1 l\beta ST + \frac{\rho_2\beta VI}{1+\theta_2 I} + \rho_1\rho_2\beta VT - (\mu+\delta)L + \rho T\right] \\
& + (\mu+\delta)\left[\frac{(1-l)\beta SI}{1+\theta_1 I} + (1-l)\rho_1\beta ST + \delta L - (\mu+\varepsilon+\gamma)I\right] + A[\gamma I - (\mu+\rho)T] \\
\leq \;& \delta\left[l\beta SI + \rho_1 l\beta ST + \rho_2\beta VI + \rho_1\rho_2\beta VT - (\mu+\delta)L + \rho T\right] \\
& + (\mu+\delta)\left[(1-l)\beta SI + (1-l)\rho_1\beta ST + \delta L - (\mu+\varepsilon+\gamma)I\right] + A[\gamma I - (\mu+\rho)T] \\
\leq \;& \left[\delta l\beta S^0 + \delta\rho_2\beta V^0 + (\mu+\delta)(1-l)\beta S^0 - (\mu+\delta+\gamma) + A\gamma\right] I \\
& + [\delta\rho_1 l\beta S^0 + \rho_1\rho_2\beta V^0 + \rho + (\mu+\delta)(1-l)\rho_1\beta S^0 - A(\mu+\rho)]T \\
= \;& \left[\delta l\beta S^0 + \delta\rho_2\beta V^0 + (\mu+\delta)(1-l)\beta S^0 - (\mu+\delta+\gamma) + A\gamma\right] I \\
= \;& \frac{(\mu+\delta)(\mu+\rho)(\mu+\varepsilon) + \mu\gamma(\mu+\delta+\rho)}{\mu+\rho}(R_0 - 1)I.
\end{aligned}$$

If $R_0 \leq 1$, then $D_t^\alpha V|_{(1.2)} \leq 0$. Further, it is obvious that the invariant set of $\{(S,\, V,\, L,\, I,\, T) \in \Omega : D_t^\alpha V|_{(1.2)} = 0\}$ is the singleton $\{E_0\}$. Therefore, it follows from LaSalle invariance principle that E_0 is globally stable if $R_0 \leq 1$. □

Now let us study the stability of the endemic equilibrium. The Jacobian matrix at equilibrium E^* is

$$J = \begin{pmatrix}
b_{11} & 0 & 0 & b_{14} & -\rho_1\beta S^* \\
p & b_{22} & 0 & b_{24} & -\rho_1\rho_2\beta V^* \\
b_{31} & b_{32} & -(\mu+\delta) & b_{34} & b_{35} \\
b_{41} & 0 & \delta & b_{44} & (1-l)\rho_1\beta S^* \\
0 & 0 & 0 & \gamma & -(\mu+\rho),
\end{pmatrix}$$

where

$$\begin{aligned}
b_{11} &= -\frac{\beta I^*}{1+\theta_1 I^*} - \rho_1\beta T^* - (\mu+p), & b_{14} &= -\frac{\beta S^*}{(1+\theta_1 I^*)^2}, \\
b_{22} &= -\frac{\rho_2\beta I^*}{1+\theta_2 I^*} - \rho_1\rho_2\beta T^* - \mu, & b_{24} &= -\frac{\rho_2\beta V^*}{(1+\theta_2 I^*)^2}, \\
b_{31} &= \frac{l\beta I^*}{1+\theta_1 I^*} + \rho_1 l\beta T^*, & b_{32} &= \frac{\rho_2\beta I^*}{1+\theta_2 I^*} + \rho_1\rho_2\beta T^*, \\
b_{34} &= \frac{l\beta S^*}{(1+\theta_1 I^*)^2} + \frac{\rho_2\beta V^*}{(1+\theta_2 I^*)^2}, & b_{35} &= \rho_1 l\beta S^* + \rho_1\rho_2\beta V^* + \rho, \\
b_{41} &= \frac{(1-l)\beta I^*}{1+\theta_1 I^*} + (1-l)\rho_1\beta T^*, & b_{44} &= \frac{(1-l)\beta S^*}{(1+\theta_1 I^*)^2} - (\mu+\varepsilon+\gamma).
\end{aligned}$$

and the corresponding characteristic equation is

$$\lambda^5 + B_1\lambda^4 + B_2\lambda^3 + B_3\lambda^2 + B_4\lambda + B_5 = 0, \tag{3.2}$$

where

$$
\begin{aligned}
B_1 &= \frac{(1-l)\beta S^*}{(1+\theta_1 I^*)^2}+\frac{pS^*}{V^*}+\frac{\Lambda}{S^*}+\mu+\delta+\rho-\varepsilon-\gamma,\\
B_2 &= (\mu+\rho)\left[\frac{(1-l)\beta S^*}{(1+\theta_1 I^*)^2}-(\mu+\varepsilon+\gamma)\right]-(1-l)\rho_1\beta\gamma S^*\\
&\quad+(\mu+\delta)\left[\frac{(1-l)\beta S^*}{(1+\theta_1 I^*)^2}+\rho-\varepsilon-\gamma\right]\\
&\quad-\delta\beta\left[\frac{lS^*}{(1+\theta_1 I^*)^2}+\frac{\rho_2 V^*}{(1+\theta_2 I^*)^2}\right]+\frac{(1-l)\beta^2 S^*}{(1+\theta_1 I^*)^2}\left(\frac{I^*}{1+\theta_1 I^*}+\rho_1 T^*\right)+\frac{p\Lambda}{V^*}\\
&\quad+\left(\frac{pS^*}{V^*}+\frac{\Lambda}{S^*}\right)\left[\frac{(1-l)\beta S^*}{(1+\theta_1 I^*)^2}+\mu+\delta+\rho-\varepsilon-\gamma\right],\\
B_3 &= \left(\mu+\delta+\frac{pS^*}{V^*}\right)\left\{(\mu+\rho)\left[\frac{(1-l)\beta S^*}{(1+\theta_1 I^*)^2}-(\mu+\varepsilon+\gamma)\right]-(1-l)\rho_1\beta\gamma S^*\right\}\\
&\quad-\delta\beta\left(\mu+\rho+\tfrac{pS^*}{V^*}\right)\left[\tfrac{lS^*}{(1+\theta_1 I^*)^2}+\tfrac{\rho_2 V^*}{(1+\theta_2 I^*)^2}\right]-\delta\rho_1\beta\gamma(lS^*+\rho_2 V^*)-\delta\rho\\
&\quad+\frac{pS^*}{V^*}(\mu+\delta)\left[\frac{(1-l)\beta S^*}{(1+\theta_1 I^*)^2}+\rho-\varepsilon-\gamma\right]+\frac{\delta\rho_2^2\beta^2 V^*}{(1+\theta_2 I^*)^2}\left(\frac{I^*}{1+\theta_2 I^*}+\rho_1 T^*\right)\\
&\quad+\beta^2 S^*\left(\frac{I^*}{1+\theta_1 I^*}+\rho_1 T^*\right)\left[\frac{\delta l+(1-l)(\mu+\delta+\frac{pS^*}{V^*})}{(1+\theta_1 I^*)^2}\right.\\
&\quad\left.+(1-l)\left(\frac{\mu+\rho}{(1+\theta_1 I^*)^2}+\rho_1\gamma\right)\right],\\
B_4 &= \left[\frac{pS^*}{V^*}(\mu+\delta)+\frac{\Lambda}{S^*}\right]\left\{(\mu+\rho)\left[\frac{(1-l)\beta S}{(1+\theta_1 I^*)^2}-(\mu+\varepsilon+\gamma)\right]-(1-l)\rho_1\beta\gamma S\right\}\\
&\quad-\delta\beta\left[\frac{lS^*}{(1+\theta_1 I^*)^2}+\frac{\rho_2 V^*}{(1+\theta_2 I^*)^2}\right]\left[\frac{pS^*}{V^*}(\mu+\rho)+\frac{\Lambda}{S^*}\right]\\
&\quad-\frac{\delta pS^*}{V^*}\left[\rho_1\beta\gamma(lS^*+\rho_2 V^*)-\rho\right]+\frac{\Lambda(\mu+\delta)}{S^*}\left[\frac{(1-l)\beta S^*}{(1+\theta_1)^2}+\rho-\varepsilon-\gamma\right]\\
&\quad+\delta\rho_2\beta^2\left(\frac{I^*}{1+\theta_2 I^*}+\rho_1 T^*\right)\left[\frac{\rho_2 V^*}{(1+\theta_2 I^*)^2}+\frac{pS^*}{(1+\theta_1 I^*)^2}\right]\\
&\quad+\beta^2 S^*\left(\frac{I^*}{1+\theta_2 I^*}+\rho_1 T^*\right)\left[\frac{\mu+\rho}{(1+\theta_1 I^*)^2}+\rho_1\gamma\right]\left[\delta l+(1-l)\left(\mu+\delta+\frac{pS^*}{V^*}\right)\right]\\
&\quad+\frac{\Lambda p}{V^*}+\frac{p\beta^2(S^*)^2}{(1+\theta_1 I^*)^2}\left(\frac{I^*}{1+\theta_1 I^*}+\rho_1 T^*\right)[(1-l)\mu+\delta],\\
B_5 &= \frac{\Lambda p}{V^*}\left\{(\mu+\rho)(\mu+\delta)\left[\frac{(1-l)\beta S^*}{(1+\theta_1)^2}-(\mu+\varepsilon+\gamma)\right]-(\mu+\delta)(1-l)\rho_1\beta\gamma S^*\right\}\\
&\quad+\frac{\delta\Lambda p}{V^*}\left\{\beta(\mu+\rho)\left[\frac{lS^*}{(1+\theta_1 I^*)^2}+\frac{\rho_2 V^*}{(1+\theta_2 I^*)^2}\right]-\rho_1\beta\gamma(lS^*+\rho_2 V^*)-\rho\right\}\\
&\quad+\delta\rho_2\beta^2\left(\frac{I^*}{1+\theta_2 I^*}+\rho_1 T^*\right)\left\{pS^*\left[\frac{\mu+\rho}{(1+\theta_1 I^*)^2}+\rho_1\gamma\right]\right.\\
&\quad\left.+\frac{\Lambda\rho_2 V^*}{S^*}\left[\frac{\mu+\rho}{(1+\theta_2 I^*)^2}+\rho_1\gamma\right]\right\}\\
&\quad+\frac{p\beta^2(S^*)^2}{V^*}\left(\frac{I^*}{1+\theta_1 I^*}+\rho_1 T^*\right)[(1-l)\mu+\delta]\left[\frac{\mu+\rho}{(1+\theta_1 I^*)^2}+\rho_1\gamma\right].
\end{aligned}
$$

Proposition 3.3. *The endemic equilibrium is locally asymptotically stable if all eigenvalues* λ_i, $(i = 1,3...5)$ *of characteristic equation (3.2) satisfy the inequality:* $|\arg(\lambda_i)| > \dfrac{\alpha\pi}{2}$.

3.3. **Numerical simulations.** In this section, we will illustrate the existence and stability of the equilibrium of system (1.2) via numerical simulations.

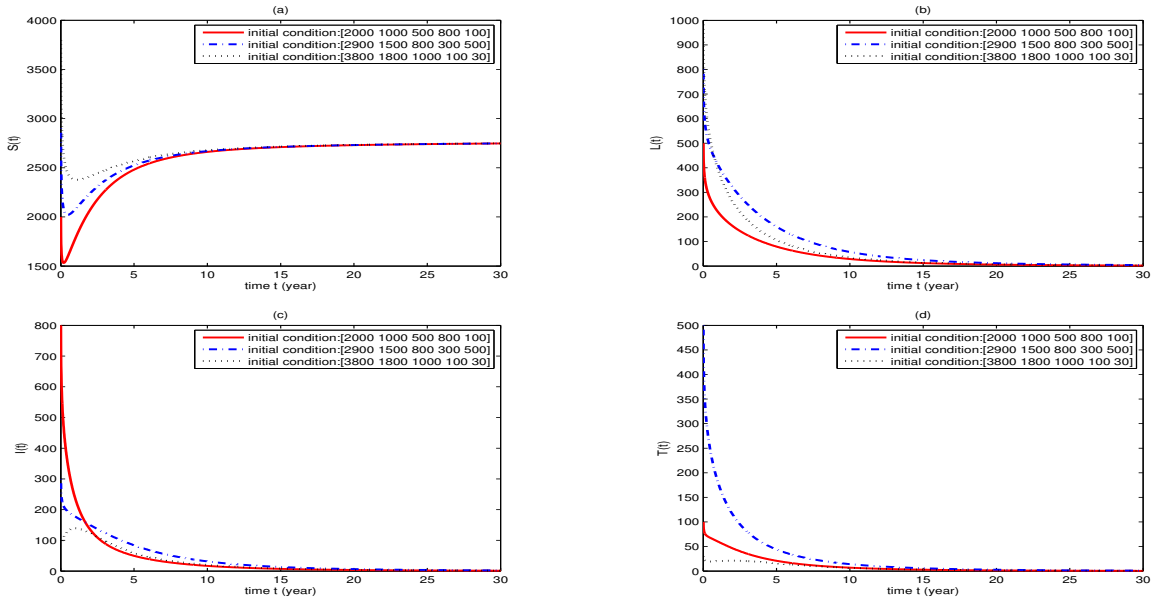

Fig. 1. (a)-(d) are the time series of the system (1.2), which show that the disease-free equilibrium E_0 is global asymptotically stable for $\alpha = 0.9$.

Example 3.4. For the following set of parameters: $\beta = 0.00002$ person^{-1}year^{-1}, $r_2 = 0.1$, $l = 0.5$, $\delta = 0.368$ year^{-1}, $\varepsilon = 0.8$ year^{-1}, $p = 0.5$, $\rho = 0.5$ year^{-1}, $\gamma = 0.1$, $\theta_1 = 0.2$, $\theta_2 = 0.2$. In this case, $R_0 = 0.3141 < 1$, and the disease-free equilibrium $E_0 = (S^0,\ V^0,\ 0,\ 0,\ 0) = (2.778 \times 10^3,\ 9.922 \times 10^4,\ 0,\ 0,\ 0)$.

Fig.1 shows that when $R_0 < 1$, the equilibrium E_0 is stable for different initial values. This is in accordance with our Theorem 3.2.

Example 3.5. For the following set of parameters: $\beta = 0.0009$ person^{-1}year^{-1}, $r_2 = 0.1$, $l = 0.9$, $\delta = 0.368$ year^{-1}, $\varepsilon = 0.5$ year^{-1}, $p = 0.5$, $\rho = 0.7$ year^{-1}, $\gamma = 0.2$, $\theta_1 = 0.2$, $\theta_2 = 0.2$, and $\alpha = 1, 0.5, 0.4$.

From Fig.2, we observe a relaxation process (sub-growth phenomena like sub-diffusion process) when $0 < \alpha < 1$. It show that the influence of order cannot be ignored.

Example 3.6. For the following set of parameters: $\beta = 0.00005$ person^{-1}year^{-1}, $r_2 = 0.1$, $l = 0.5$, $\delta = 0.368$ year^{-1}, $\varepsilon = 0.17$ year^{-1}, $p = 0.5$, $\rho = 0.7$ year^{-1}. $\gamma = 0.1$.

(1) $\theta_2 = 0$, Fig.3.1 shows the dynamics with the initial value $[S(0),\ V(0),\ L(0),\ I(0),\ T(0)]$ = $[2000,\ 1800,\ 1800,\ 800,\ 300]$ for $\theta_1 = 0,\ 0.2$.

(2) $\theta_1 = 0$, Fig.3.2 shows the dynamics with the initial value $[S(0),\ V(0),\ L(0),\ I(0),\ T(0)]$ = $[2000,\ 1800,\ 1800,\ 800,\ 300]$ for $\theta_2 = 0,\ 0.2$.

From Fig.3.1 and Fig.3.2, we can see that the parameter θ_1 and θ_2 is sensitive to the system.

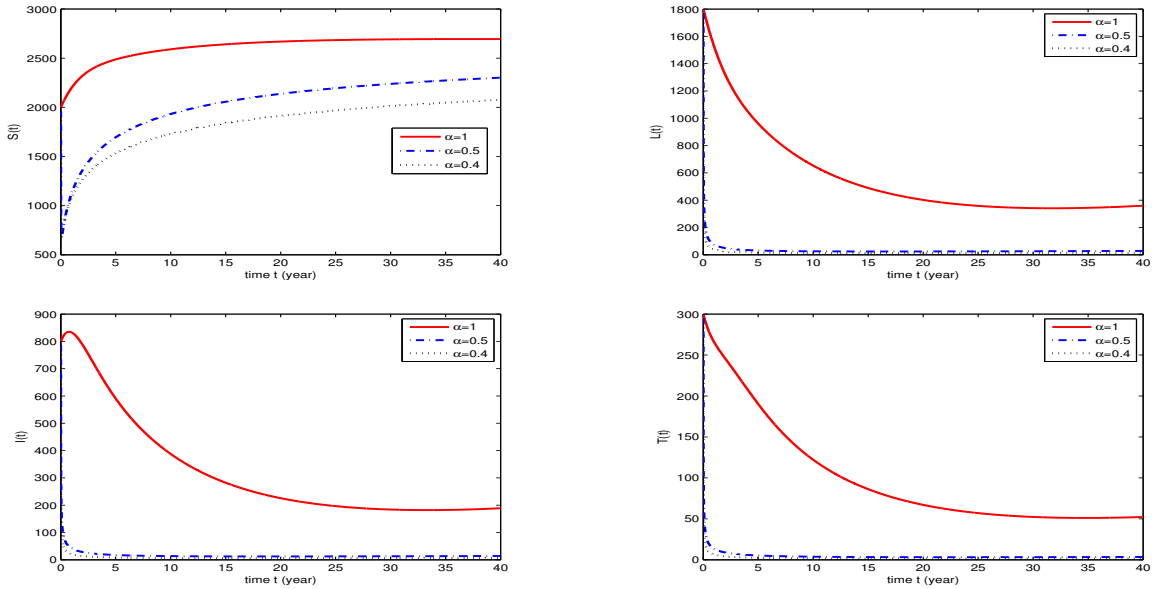

Fig. 2. (a)-(d) are the time series of the system (1.2), which show that the endemic equilibrium E^* is local asymptotically stability. (the initial conditions: [2000, 3800, 1800, 800, 300])

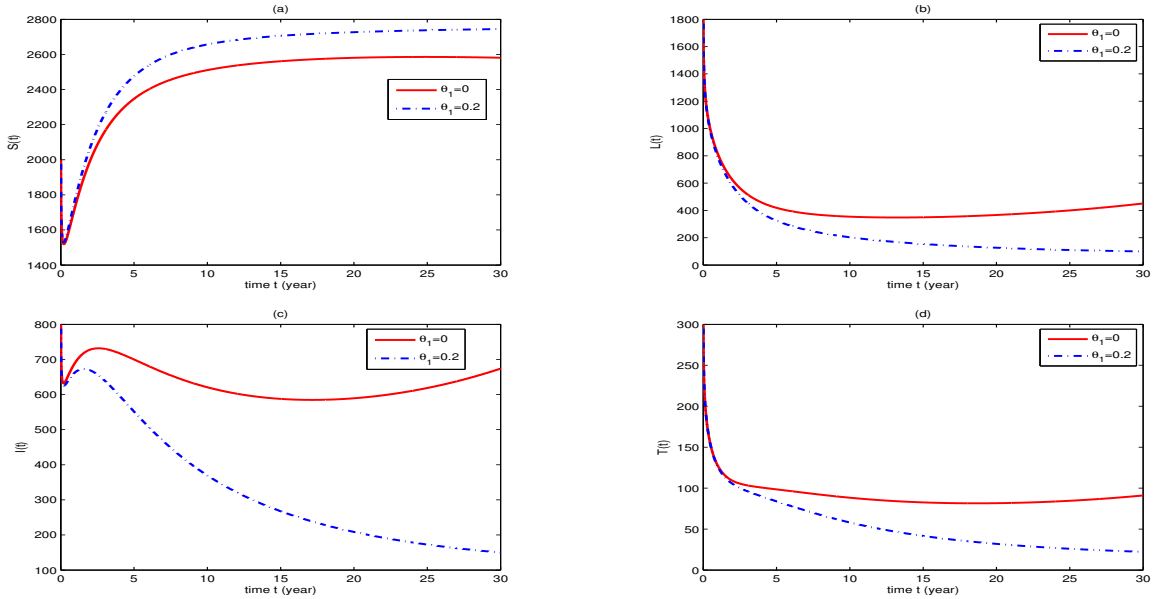

Fig. 3.1. (a)-(d) are the time series of system (1.2), which show that the influence of θ_1 when $\alpha = 0.9$. (the initial conditions: [2000, 1800, 1800, 800, 300]).

4. THE OPTIMAL CONTROL PROBLEM

In this section, the initial model is extended to include an optimal control problem for the transmission dynamics of tuberculosis. The goal is to show that time-dependent anti-TB control technologies can be implemented at minimal cost. In order to understand under what circumstances tuberculosis can be controlled or reduced, we implemented the optimal control theory.

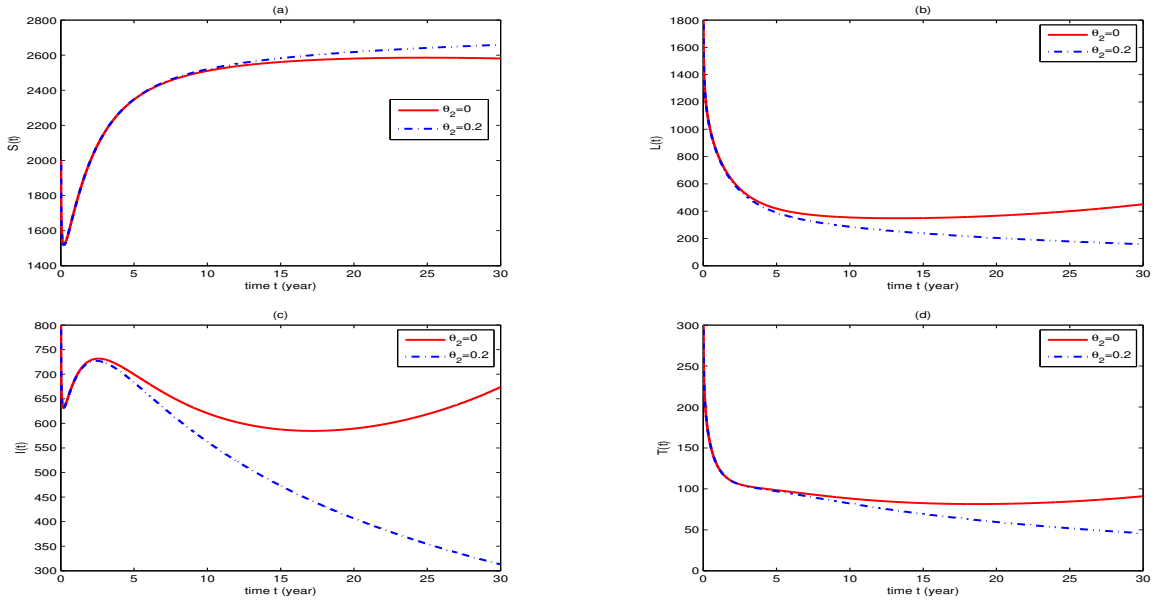

Fig. 3.2. (a)-(d) are the time series of system (1.2), which show that the influence of θ_2 when $\alpha = 0.9$. (the initial conditions: [2000, 1800, 1800, 800, 300])

Three intervention strategies, called controls, are included in system (1.2). We used $u_1(t)$ instead of a constant vaccination rate p; $u_2(t)$ was used to replace the fixed rate of successful treatment ρ; use $u_3(t)$ instead of fixed treatment rate γ.

Now, we describe the fractional order equations of the controlled model:

$$\begin{cases} D^{\alpha}S(t) = \Lambda - \dfrac{\beta SI}{1+\theta_1 I} - \rho_1\beta ST - (\mu + u_1(t))S, \\ D^{\alpha}V(t) = u_1(t)S - \dfrac{\rho_2\beta VI}{1+\theta_2 I} - \rho_1\rho_2\beta VT - \mu V, \\ D^{\alpha}L(t) = \dfrac{l\beta SI}{1+\theta_1 I} + \rho_1 l\beta ST + \dfrac{\rho_2\beta VI}{1+\theta_2 I} + \rho_1\rho_2\beta VT - (\mu+\delta)L + u_2(t)T, \\ D^{\alpha}I(t) = \dfrac{(1-l)\beta SI}{1+\theta_1 I} + (1-l)\rho_1\beta ST + \delta L - (\mu + \varepsilon + u_3(t))I, \\ D^{\alpha}T(t) = u_3(t)I - (\mu + u_2(t))T. \end{cases} \tag{4.1}$$

The optimal control problem of objective (cost) function is given:

$$J(u_1,\ u_2,\ u_3) = \int_0^{t_f} \left[B_1L(t) + B_2I(t) + B_3T(t) + B_4u_1^4 + B_5u_2^2 + B_6u_3^2\right] \mathrm{d}t,$$

$B_i (i = 1, 2, \cdots, 6)$ are the weight constants and control measures of infected TB patients. Because of the size and importance of the target feature, they can be selected to balance the cost factor.

We hypothesize that there may be practical limitations on the maximum rate at which individuals can be vaccinated or treated over a period of time and achieve treatment success. We seek optimal controls u_1, u_2 and u_3 in U such that

$$\min J(u_1,\ u_2,\ u_3), \tag{4.2}$$

where $U = \{(u_1,\ u_2,\ u_3) | u_i$ are Lebesgue integrable, $0 \le u_i \le u_{i\max}, i = 1, 2, 3\}$ is the control set.

4.1. **The existence of an optimal control.** In this section, we will study the sufficient condition for the existence of an optimal control of our system (4.1). We refer to Theorem III 4.1 and its Corollary in [43].

For convenience, let $\vec{x} = [S,\ V,\ L,\ I,\ T]^T$ and $\vec{u} = [u_1,\ u_2\ ,u_3]^T$ denote the vector of system states variables and controls variables, respectively.

Theorem 4.1. *There exists an optimal control* $(u_1^*,\ u_2^*,\ u_3^*)$ *to problem (4.2).*

Proof. From Theorem III 4.1 and its Corollary in [43], we let $r(t,\vec{x},\vec{u})$ be the right-hand side of (4.1). We need to proof the following conditions are satisfied:

(1) r is of class C^1 and there exists a constant M such that

$$|r(t,0,0)| \le M, \quad |r_{\vec{x}}(t,\vec{x},\vec{u})| \le M(1+|\vec{u}|), \quad |r_{\vec{u}}(t,\vec{x},\vec{u})| \le M;$$

(2) The admissible set F of all solutions to system (4.1) with corresponding control in U is nonempty;

(3) $r(t,\vec{x},\vec{u}) = a(t,\vec{x}) + b(t,\vec{x})\vec{u}$;

(4) The control set $\tilde{U} = [0,u_{1\max}] \times [0,u_{2\max}] \times [0,u_{3\max}]$ is closed, convex and compact;

(5) The integrand of the objective functional is convex in $\tilde{U}$.

Denote

$$r(t,\vec{x},\vec{u}) = \begin{pmatrix} \Lambda - \frac{\beta SI}{1+\theta_1 I} - \rho_1\beta ST - (\mu+u_1)S \\ u_1 S - \frac{\rho_2\beta VI}{1+\theta_2 I} - \rho_1\rho_2\beta VT - \mu V \\ \frac{l\beta SI}{1+\theta_1 I} + \rho_1 l\beta ST + \frac{\rho_2\beta VI}{1+\theta_2 I} + \rho_1\rho_2\beta VT - (\mu+\delta)L + u_2 T \\ \frac{(1-l)\beta SI}{1+\theta_1 I} + (1-l)\rho_1\beta ST + \delta L - (\mu+\varepsilon+u_3)I \\ u_3 I - (\mu+u_2)T \end{pmatrix}.$$

Obviously, r is of class C^1 and $|r(t,0,0)| = \Lambda$. And we have

$$|r_{\vec{x}}(t,\vec{x},\vec{u})| = \left| \begin{pmatrix} c_{11} & 0 & 0 & c_{14} & -\rho_1\beta S \\ p & c_{22} & 0 & c_{24} & -\rho_1\rho_2\beta V \\ c_{31} & a_{32} & -(\mu+\delta) & c_{34} & c_{35} \\ c_{41} & 0 & \delta & c_{44} & (1-l)\rho_1\beta S \\ 0 & 0 & 0 & \gamma & -(\mu+\rho) \end{pmatrix} \right|,$$

where

$$\begin{aligned} c_{11} &= -\frac{\beta I}{1+\theta_1 I} - \rho_1\beta T - (\mu+p), & c_{14} &= -\frac{\beta S}{(1+\theta_1 I)^2}, \\ c_{22} &= -\frac{\rho_2\beta I}{1+\theta_2 I} - \rho_1\rho_2\beta T - \mu, & c_{24} &= -\frac{\rho_2\beta V}{(1+\theta_2 I)^2}, \\ c_{31} &= \frac{l\beta I}{1+\theta_1 I} + \rho_1 l\beta T, & c_{32} &= \frac{\rho_2\beta I}{1+\theta_2 I} + \rho_1\rho_2\beta T, \\ c_{34} &= \frac{l\beta S}{(1+\theta_1 I)^2} + \frac{\rho_2\beta V}{(1+\theta_2 I)^2}, & c_{35} &= \rho_1 l\beta S + \rho_1\rho_2\beta V + \rho, \\ c_{41} &= \frac{(1-l)\beta I}{1+\theta_1 I} + (1-l)\rho_1\beta T, & c_{44} &= \frac{(1-l)\beta S}{(1+\theta_1 I)^2} - (\mu+\varepsilon+\gamma). \end{aligned}$$

and

$$|r_{\vec{u}}(t,\vec{x},\vec{u})| = \left| \begin{pmatrix} -S & 0 & 0 \\ S & 0 & 0 \\ 0 & T & 0 \\ 0 & 0 & -I \\ 0 & -T & I \end{pmatrix} \right|.$$

Since S, V, L, I, T are bounded, then condition (1) holds, which further implies that condition (2) holds.

In addition, through simple calculation shows that condition (3) satisfies. And obviously condition (4) is satisfied. According to Theorem 3.1 in [44], condition (5) is satisfied. □

4.2. **Characterization of an optimal control.** Next, we obtain the necessary conditions to utilize Pontryagin's Maximum Principle [45, 46] and find the optimal solution.

Note that the Hamiltonian function for our problem is given by:

$$\begin{aligned} & H(S,V,L,I,T,u_1,u_2,u_3,\lambda) \\ = \; & B_1L(t)+B_2I(t)+B_3T(t)+B_4u_1^4+B_5u_2^2+B_6u_3^2 \\ + \; & \lambda_1\left[\Lambda-\frac{\beta SI}{1+\theta_1 I}-\rho_1\beta ST-(\mu+u_1)S\right] \\ + \; & \lambda_2\left[u_1S-\frac{\rho_2\beta VI}{1+\theta_2 I}-\rho_1\rho_2\beta VT-\mu V\right] \\ + \; & \lambda_3\left[\frac{l\beta SI}{1+\theta_1 I}+\rho_1 l\beta ST+\frac{\rho_2\beta VI}{1+\theta_2 I}+\rho_1\rho_2\beta VT-(\mu+\delta)L+u_2T\right] \\ + \; & \lambda_4\left[\frac{(1-l)\beta SI}{1+\theta_1 I}+(1-l)\rho_1\beta ST+\delta L-(\mu+\varepsilon+u_3)I\right] \\ + \; & \lambda_5[u_3I-(\mu+u_2)T], \end{aligned}$$

where, $\lambda = (\lambda_1,\ \lambda_2,\ \lambda_3,\ \lambda_4,\ \lambda_5)$ is known as adjoint variable.

Theorem 4.2. *Let S^*,V^*,L^*,I^*,T^* be optimal state solutions with associated optimal control variable $(u_1^*,\ u_2^*,\ u_3^*)$ for the optimal control problem (4.1)-(4.2). Then there exist adjoint variables λ_i, for $i=1,2,\cdots,5$, satisfying*

$$\begin{cases} \frac{d\lambda_1}{dt} = \frac{\lambda_1\beta I}{1+\theta_1 I}+\lambda_1\rho_1\beta T+\lambda_1(\mu+u_1)-\lambda_2u_1-\frac{\lambda_3 l\beta I}{1+\theta_1 I}-\lambda_3\rho_1 l\beta T-\frac{\lambda_4(1-l)\beta I}{1+\theta_1 I}-\lambda_4(1-l)\rho_1\beta I, \\ \frac{d\lambda_2}{dt} = \frac{\lambda_2\rho_2\beta I}{1+\theta_2 I}+\lambda_2\rho_1\rho_2\beta T+\lambda_2\mu-\frac{\lambda_3\rho_2\beta I}{1+\theta_2 I}-\lambda_3\rho_1\rho_2\beta T, \\ \frac{d\lambda_3}{dt} = -B_1+\lambda_3(\mu+\delta)-\lambda_4\delta, \\ \frac{d\lambda_4}{dt} = -B_2+\frac{\lambda_1\beta S}{(1+\theta_1 I)^2}+\frac{\lambda_2\rho_2\beta V}{(1+\theta_2 I)^2}-\frac{\lambda_3 l\beta S}{(1+\theta_1 I)^2}-\frac{\lambda_3\rho_2\beta V}{(1+\theta_2 I)^2}-\frac{\lambda_4(1-l)\beta S}{(1+\theta_1 I)^2}+\lambda_4(\mu+\varepsilon+u_3)-\lambda_5u_3, \\ \frac{d\lambda_5}{dt} = -B_3+\lambda_1\rho_1\beta S+\lambda_2\rho_1\rho_2\beta V-\lambda_3\rho_1 l\beta S-\lambda_3\rho_1\rho_2\beta V \\ \qquad -\lambda_3u_2-\lambda_4(1-l)\rho_1\beta S+\lambda_5(\mu+u_2). \end{cases}$$

with transversal conditions (or boundary conditions)

$$\lambda_i(t_f)=0,\ i=1,2,\cdots,5.$$

Furthermore, optimal control $u_i^*, (i = 1,2,3)$ *is given by*

$$\begin{aligned} u_1^* &= \min\left\{\max\left\{0,\ \left(\frac{(\lambda_1-\lambda_2)S^*}{4B_4}\right)^{\frac{1}{3}}\right\},\ u_{1\max}\right\},\\ u_2^* &= \min\left\{\max\left\{0,\ \frac{(\lambda_5-\lambda_3)T^*}{2B_5}\right\},\ u_{2\max}\right\},\\ u_3^* &= \min\left\{\max\left\{0,\ \frac{(\lambda_4-\lambda_5)T^*}{2B_6}\right\},\ u_{3\max}\right\}. \end{aligned} \tag{4.3}$$

Proof. In order to determine adjoint equations and transversal conditions, we use Hamiltonian. The adjoint system can be derived from Pontryagin's Maximum Principle

$$\begin{cases} \frac{\mathrm{d}\lambda_1}{dt} = -\frac{\partial H}{\partial S},\\ \frac{\mathrm{d}\lambda_2}{dt} = -\frac{\partial H}{\partial V},\\ \frac{\mathrm{d}\lambda_3}{dt} = -\frac{\partial H}{\partial L},\\ \frac{\mathrm{d}\lambda_4}{dt} = -\frac{\partial H}{\partial I},\\ \frac{\mathrm{d}\lambda_5}{dt} = -\frac{\partial H}{\partial T}, \end{cases}$$

with $\lambda_i(t_f) = 0$. Let $\dfrac{\partial H}{\partial u_1} = \dfrac{\partial H}{\partial u_2} = \dfrac{\partial H}{\partial u_3} = 0$, we can get the formula of Eq.(4.3). □

4.3. **Numerical simulations.** In this section, we discuss the numerical simulation of model (4.1) with the cost function of the optimal control strategy.

Example 4.3. For the following set of parameters: $\beta = 0.003$ person^{-1}year^{-1}, $r_2 = 0.2$, $l = 0.9$, $\delta = 0.00368$ year^{-1}, $\varepsilon = 0.17$ year^{-1}, $\theta_1 = 0.2$, $\theta_2 = 0.2$.

As expected, the results shown in Fig.4(c) clearly indicate that the optimal control results are very effective in the control of patients infected with latent TB; In Fig.4(e), the number of people receiving treatment dropped sharply in the first four years, and then dropped sharply, this is due to treatment that controls u_3 to zero after 4 years. And Fig.4 shows a slight increase in the intervention strategy after 4 years.

Example 4.4. For the following set of parameters: $\beta = 0.003$ person^{-1}year^{-1}, $r_2 = 0.2$, $l = 0.9$, $\delta = 0.00368$ year^{-1}, $\varepsilon = 0.17$ year^{-1}, $\theta_1 = 0.2$, $\theta_2 = 0.2$.

Fig.5 shows that the optimal control of system (4.1) is bang-bang type, and no singular solution is found.

5. Discussion

In this paper, a fractional-order tuberculosis model with incomplete treatment was constructed and investigated. In Section 3, we obtained the basic reproduction number R_0, and the sufficient conditions for the existence and stability of E_0 and E^*. If $R_0 < 1$, then the disease-free equilibrium E_0 of system (1.2) is global asymptotically stable within Ω; If $R_0 > 1$, then the endemic equilibrium appears and is local asymptotically stable under certain conditions. In Section 4, we presented the formulation of the optimal control problems, investigated the existence of an optimal control function and derived an optimal system characterizing the optimal control. Through numerical simulation, we have the following results.

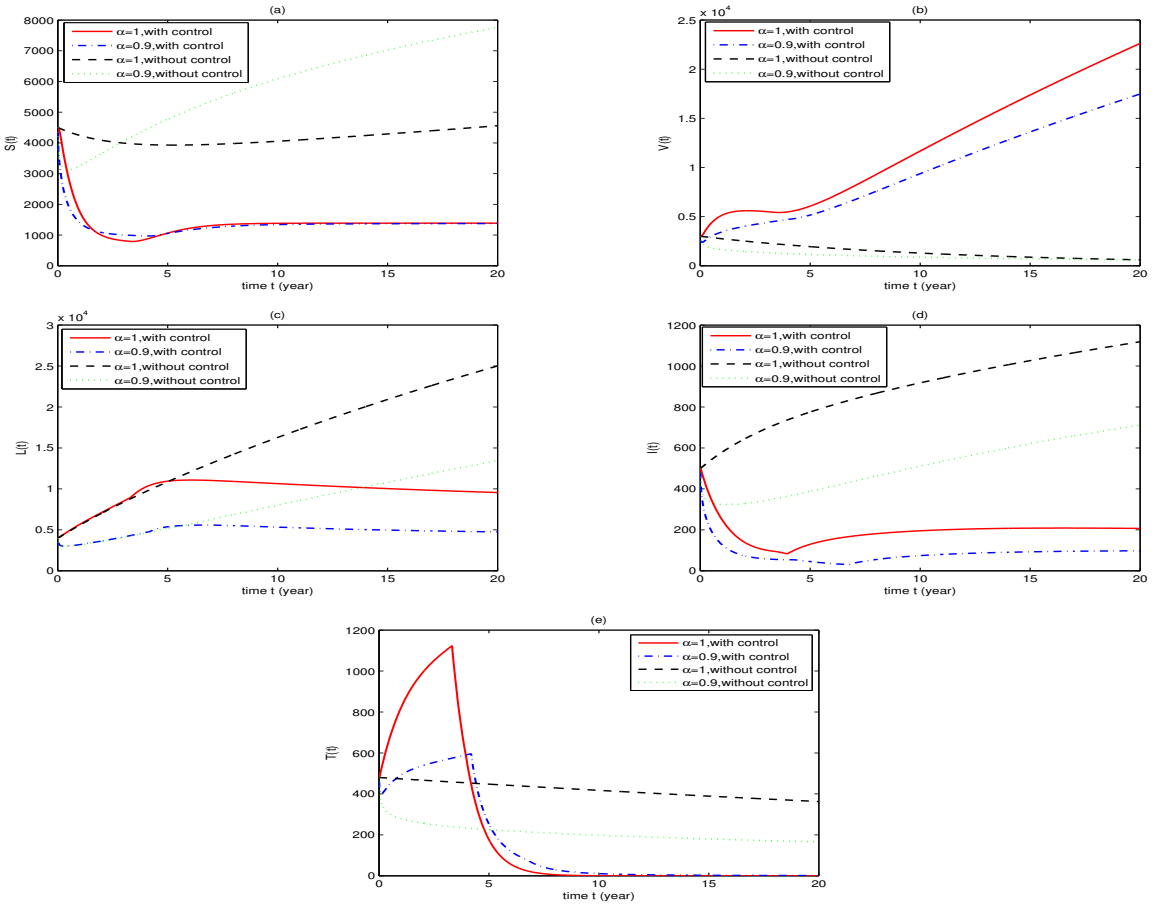

Fig. 4. (a)-(e) are the time series of the system (4.1), which show that with and without controls for $\alpha = 1$ and 0.9, weight constants are $B_1 = 20$, $B_2 = 100$, $B_3 = 200$, $B_4 = 100$, $B_5 = 8000$, $B_6 = 150$. (the initial conditions: [4500, 3000, 4000, 500, 480], the red and $'-'$ line: α=1, with control; the blue and $'-.-.'$ line: α=0.9 with control; the black and $'--'$ line: α=1 without control; the green and $'...'$ line: α=0.9 without control)

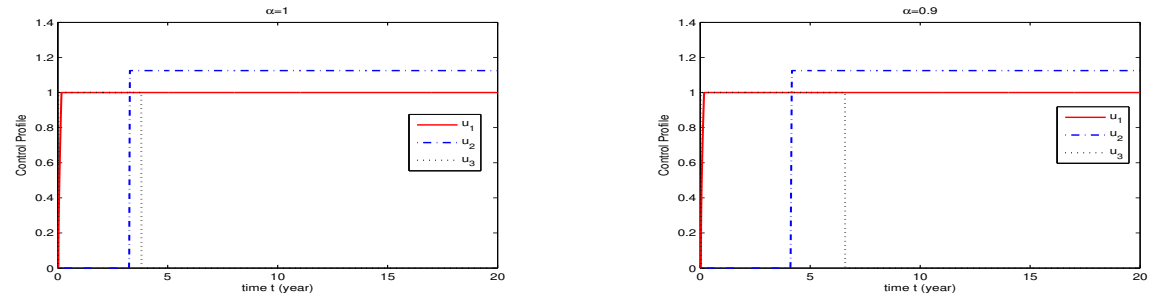

Fig. 5. Three optimal control strategies profiles weight constants are $B_1 = 20$, $B_2 = 100$, $B_3 = 200$, $B_4 = 100$, $B_5 = 8000$, $B_6 = 150$ (the initial conditions: [4500, 3000, 4000, 500, 480]).

$\Diamond$ Fig.1 shows that the disease-free equilibrium E_0 of system (1.2) is indeed globally stable when $R_0 < 1$.

$\Diamond$ Fig.2 shows that the endemic equilibrium E^* system (1.2) is local globally stable.

$\Diamond$ Fig.3.1 and Fig.3.2 show that the impact of θ_1 and θ_2 on the system is crucial.

$\Diamond$ Fig.4 shows that vaccination and treatment strategies effectively reduce the spread of TB diseases, especially we can use the lowest cost to obtain the maximum disease control.

Remark 5.1. If $\alpha = 1$ and $\theta_1 = \theta_2 = 0$, then system (1.2) degenerates to the model in [31].

In this paper, the effect of time delay is not considered, and we leave it as our future work.

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