Optimal control for a fractional tuberculosis infection model including the impact of diabetes and resistant strains

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ABSTRACT

The objective of this paper is to study the optimal control problem for the fractional tuberculosis (TB) infection model including the impact of diabetes and resistant strains. The governed model consists of 14 fractional-order (FO) equations. Four control variables are presented to minimize the cost of interventions. The fractional derivative is defined in the Atangana-Baleanu-Caputo (ABC) sense. New numerical schemes for simulating a FO optimal system with Mittag-Leffler kernels are presented. These schemes are based on the fundamental theorem of fractional calculus and Lagrange polynomial interpolation. We introduce a simple modification of the step size in the two-step Lagrange polynomial interpolation to obtain stability in a larger region. Moreover, necessary and sufficient conditions for the control problem are considered. Some numerical simulations are given to validate the theoretical results.

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Introduction

A new study suggests that millions of people with high blood sugar may be more likely to develop tuberculosis (TB) than previously expected. TB is a severe infection that is caused by bacteria in the lungs and kills many people each year, in addition to HIV/AIDS and malaria, according to the Daily Mail website [1]. In 2017, according to the World Health Organization nearly 10 million people were infected with TB [2]. Experts are concerned that a global explosion in the number of diabetes cases will put millions of people at risk [3].

Many mathematical models have been proposed to elucidate the patterns of TB [4–7]. Recently, Khan et al., [8], presented a new fractional model for tuberculosis. In addition, several papers considered modeling TB with diabetes; see, for example, [9–12]. Recently, Carvalho and Pinto presented non-integer-order analysis of the impact of diabetes and resistant strains in a model of TB infection [13]. Fractional-order (FO) models provide more accurate and deeper information about the complex behaviors of various diseases than can classical integer-order models. FO systems are superior to integer-order systems due to their hereditary properties and description of memory [14–28]. Fractional optimal control problems (FOCPs) are optimal control problems associated with fractional dynamic systems. Fractional optimal control theory is a very new topic in mathematics. FOCPs may be defined in terms of different types of fractional derivatives. However, the most important types of fractional derivatives are the Riemann-Liouville and Caputo fractional derivatives [29–40]. In addition, the theory of FOCPs has been under development. Recently, some interesting real-life models of optimal control problems (OCPs) were presented elsewhere [41–52].

A new concept of differentiation was introduced in the literature whereby the kernel was converted from non-local singular to non-local and non-singular. One of the great advantages of this new kernel is its ability to portray fading memory as well as the well-defined memory of the system under investigation. A new FO derivative, based on the generalized Mittag fading memory as well as the well-defined memory of the system under investigation. A new FO derivative, based on the generalized Mittag-Leffler function, is defined as in [14]:

\[
\mathcal{B}_0^\alpha \mathcal{D}_t^\gamma g(t) = \frac{\mathcal{B}(t)}{(1 - \alpha)} \int_0^t (t - q)^{\gamma - 1} g(q) dq, \quad 0 < \alpha \leq 1.
\]  

\[ (1) \]

Definition 1. The Liouville-Caputo FO derivative is defined as in [53]:

\[
\mathcal{B}_0^\alpha \mathcal{D}_t^\gamma g(t) = \frac{B(x)}{(1 - \alpha)} \int_0^t (E_x(-x)(t - q)^{\gamma - 1} g(q)) dq.
\]

\[ (2) \]

where \( B(x) = 1 - x + \frac{x}{1!} \) is the normalization function.

Definition 2. The Atangana-Baleanu fractional derivative in the Liouville-Caputo sense is defined as in [14]:

\[
\mathcal{A}_0^\alpha D_t^\gamma g(t) = \frac{\mathcal{B}(x)}{B(x)} \int_0^t (t - q)^{\gamma - 1} g(q) dq.
\]

They found that when \( \alpha \) is zero, they recovered the initial function, and if \( \alpha \) is 1, they obtained the ordinary integral. In addition, they computed the Laplace transform of both derivatives and obtained the following:

\[
\mathcal{L}\{\mathcal{A}_0^\alpha D_t g(t)\} = \frac{B(x)g(p)^{p^\alpha} - p^{\alpha - 1} g(0)}{(1 - \alpha)(p^{\alpha} + \frac{\alpha}{\Gamma(x)})}.
\]

Theorem 1. For a function \( g \in C[a, b] \), the following result holds [9]:

\[
\|\mathcal{A}_0^\alpha D_t^\gamma g(t)\| < \frac{B(x)}{(1 - \alpha)} \|g(t)\|, \text{ where } \|g(t)\| = \max_{t \in [a, b]} |g(t)|.
\]

Further, the Atangana–Baleanu-Caputo derivatives fulfill the Lipschitz condition [9]:

\[
\|\mathcal{A}_0^\alpha D_t^\gamma g_1(t) - \mathcal{A}_0^\alpha D_t^\gamma g_2(t)\| < \frac{\alpha}{\Gamma(x)} \|g_1(t) - g_2(t)\|.
\]

Fractional model for TB infection including the impact of diabetes and resistant strains

In this section, we study fractional optimal control for TB infection including the impact of diabetes and resistant strains, as given in Carvalho and Pinto [13]. So that the reader can make sense of the model, Fig. 1 shows the flowchart of the model as given in Carvalho and Pinto [13]. The fractional derivative here is defined in the ABC sense. We add four control functions, \( u_1, u_2, u_3 \) and \( u_4 \), and four real positive model constants, \( c_0 i = 1.2.3.4 \) and \( c_0 i e (0, 1) \). These controls are given to prevent the failure of treatment in \( I_1, I_2, I_3 \) and \( I_4 \), e.g., patients’ health care providers encourage them to complete the treatments by taking TB and diabetes medications regularly. This model consists of fourteen classes. Let us consider the population to be divided into diabetic (index 1) and non-diabetic
(index 2). Then, we have susceptible individuals ($S_2$ and $S_1$), individuals exposed and sensitive to TB ($E_2$ and $E_1$), individuals exposed and resistant to TB ($E_{2R}$ and $E_{1R}$), individuals infected with and sensitive to TB ($I_2$ and $I_1$), individuals infected with and resistant to TB ($I_{2R}$ and $I_{1R}$), individuals recovering from and sensitive to TB ($R_2$ and $R_1$), and individuals recovering from and resistant to TB ($R_{2R}$ and $R_{1R}$). All the parameters for the modified model in Table 1, depend on the FO because the use of the constant parameter $\alpha$ instead of an integer parameter can lead to better results, as one has an extra degree of freedom [40]. The main assumption of this model is that the total population $N$ is a constant in time, i.e., the birth and death rates are equal and $\alpha_0^2 = 0$. The resulting model with four controls is given as follows:

$$\begin{align*}
\text{ARC } D^\alpha_0 I_{21} &= (1 - \xi)P_2 \theta_2 S_2 + (1 - r_2) (k_{21}^P + \sigma_2 \theta_2) E_2 + \tau_1 x_2^2 I_{12} + \delta_2^1 R_2 - (\eta_2^2 + \gamma_2^2 + \mu^2 + d_2^2 + \omega d_2) I_{21}, \\
\text{ARC } D^\alpha_0 I_{2R} &= \xi P_2 \theta_2 S_2 + (1 - r_2) (k_2^P + \sigma_2 \theta_2) E_{2R} + \eta_2^I I_{22} + \tau_1 x_2^2 I_{1R} + \delta_2^2 R_{2R} - (\gamma_2^2 + \mu^2 + d_2^2 + \omega d_2 u_2) I_{2R}, \\
\text{ARC } D^\alpha_0 R_{11} &= \gamma_1^0 I_{11} + \omega d_1 u_1 I_{11} - \sigma_1 (1 - \delta_1^1) \lambda_1 R_{11} - (\delta_1^1 + \xi + \delta_1^2 + \mu^2) R_{11}, \\
\text{ARC } D^\alpha_0 R_{1R} &= \gamma_1^2 I_{1R} + \omega d_1 u_1 I_{1R} - \sigma_1 (1 - \delta_1^1) \lambda_1 R_{1R} - (\delta_1^1 + \xi + \mu^2) R_{1R},
\end{align*}$$

where

$$\lambda_t = \frac{\beta I_{1s} + \mu_1 I_{1s} + \mu d_1 I_{1R}}{N}.$$

**Control problem formulation**

Let us consider the state system presented in Eqs. (3)–(16), in $R^{14}$, with the set of admissible control functions

$$\Omega = \{(u_1(\cdot), u_2(\cdot), u_3(\cdot), u_4(\cdot)) | u_i \text{ is Lebesgue measurable on } [0, 1],$$

$$0 \leq u_1(\cdot), u_2(\cdot), u_3(\cdot), u_4(\cdot) \leq 1, \forall t \in [0, T_f], \quad i = 1, 2, 3, 4,$$

where $T_f$ is the final time and $u_1(\cdot), u_2(\cdot), u_3(\cdot)$ and $u_4(\cdot)$ are controls functions.
subject to the constraint

\begin{align*}
&\sum_{a} a^{*} D^{*}_{i} S_{1} = \xi_{1}, \quad \sum_{a} a^{*} D^{*}_{i} S_{2} = \xi_{2}, \quad \sum_{a} a^{*} D^{*}_{i} E_{1s} = \xi_{3}, \\
&\sum_{a} a^{*} D^{*}_{i} E_{IR} = \xi_{4}, \quad \sum_{a} a^{*} D^{*}_{i} E_{2s} = \xi_{5}, \quad \sum_{a} a^{*} D^{*}_{i} E_{2s} = \xi_{6}, \\
&\sum_{a} a^{*} D^{*}_{i} I_{1s} = \xi_{7}, \quad \sum_{a} a^{*} D^{*}_{i} I_{1s} = \xi_{8}, \quad \sum_{a} a^{*} D^{*}_{i} I_{1s} = \xi_{9}, \\
&\sum_{a} a^{*} D^{*}_{i} I_{2s} = \xi_{10}, \quad \sum_{a} a^{*} D^{*}_{i} I_{2s} = \xi_{11}, \quad \sum_{a} a^{*} D^{*}_{i} R_{1s} = \xi_{12}, \\
&\sum_{a} a^{*} D^{*}_{i} R_{2s} = \xi_{13}, \quad \sum_{a} a^{*} D^{*}_{i} R_{2s} = \xi_{14}.
\end{align*}

where

\[
\xi_{i} = \xi_{1}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t).
\]

For $i = 1, \ldots, 14$, and the following initial conditions are satisfied:

\[
S_{1}(0) = S_{01}, \quad S_{2}(0) = S_{02}, \quad E_{1s}(0) = E_{10}, \quad E_{1s}(0) = E_{10}, \quad E_{2s}(0) = E_{20}, \quad E_{2s}(0) = E_{20}, \quad I_{1s}(0) = I_{10}, \quad I_{1s}(0) = 1_{10}, \quad I_{2s}(0) = I_{20}, \quad I_{2s}(0) = I_{20}, \quad R_{1s}(0) = R_{10}, \quad R_{1s}(0) = R_{10}, \quad R_{2s}(0) = R_{20}.
\]

To define the FOCM, consider the following modified cost function [31]:

\[
J = \int_{0}^{T_{f}} \left[ H_{0}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t) \\
- \sum_{i=1}^{14} \left( i_{i} \xi_{i}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t) \right) \right] dt.
\]

(19)

where $j = 1, 2, 3, 4, \text{ and } i = 1, \ldots, 14$.

The Hamiltonian is given as follows:

\[
H_{0}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t) = \eta_{1}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t)
\]

\[
+ \sum_{i=1}^{14} \left( i_{i} \xi_{i}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t) \right) \right] dt.
\]

(20)

The objective function is defined as follows:

\[
J(u_{1}, u_{2}, u_{3}, u_{4}) = \int_{0}^{T_{f}} \left[ I_{1s}(I_{1s} + I_{1s}) + I_{2s} + I_{2s} \right] B_{1}\sum_{i}^{14} \left( i_{i} \xi_{i}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t) \right) dt.
\]

(17)

where $B_{1}$, $B_{2}$, $B_{3}$, and $B_{4}$ are the measure of the relative cost of the interventions associated with the controls $u_{1}$, $u_{2}$, $u_{3}$, and $u_{4}$.

Then, we find the optimal controls $u_{1}$, $u_{2}$, $u_{3}$, and $u_{4}$ that minimize the cost function

\[
J(u_{1}, u_{2}, u_{3}, u_{4}) = \int_{0}^{T_{f}} \left[ \eta_{1}(S_{1}, S_{2}, E_{1s}, E_{1s}, E_{2s}, I_{1s}, I_{1s}, I_{2s}, I_{2s}, R_{1s}, R_{1s}, R_{2s}, R_{2s}, u_{1}, u_{2}, u_{3}, u_{4}, t) \right] dt.
\]

(18)

(22)

The parameters of systems (3)-(16) and their descriptions [13].

| Parameter | Description | Values |
|-----------|-------------|--------|
| $A^{*}$  | Recruitment rate | 667,685 |
| $x^{0}$  | Diabetes acquisition rate | 0.58 yr⁻¹ |
| $\gamma$ | Effective contact rate for TB infection | (5, 8, 9) |
| $\varepsilon$ | Modification parameter | 1.1 |
| $\varepsilon$ | Modification parameter | 1.1 |
| $\omega$ | Modification parameter | 2 |
| $\mu$ | Rate of natural death | +∞ yr⁻¹ |
| $\delta$ | Rate of TB infection among diabetic individuals | 0.04 |
| $P_{1}$ | Rate of TB infection among non-diabetic individuals | 0.03 |
| $P_{2}$ | Rate of TB infection among diabetic individuals | 0.06 |
| $R_{1}$ | Non-diabetic individuals’ chemoprophylaxis rate | 0 yr⁻¹ |
| $R_{2}$ | Diabetic individuals’ chemoprophylaxis rate | 0 yr⁻¹ |
| $\sigma_{1}$ | Non-diabetic individuals’ degree of immunity | 0.75 P |
| $\sigma_{2}$ | Diabetic individuals’ degree of immunity | 0.7 P |
| $k_{1}$ | Non-diabetic individuals’ rate of endogenous reactivation | 0.0013 yr⁻¹ |
| $k_{2}$ | Diabetic individuals’ rate of endogenous reactivation | 2 yr⁻¹ |
| $\gamma_{11}$ | Non-diabetic individuals’ sensitive TB infection recovery rate | 0.7372 yr⁻¹ |
| $\gamma_{12}$ | Non-diabetic individuals’ resistant TB infection recovery rate | 0.7372 yr⁻¹ |
| $\gamma_{21}$ | Diabetic individuals’ sensitive TB infection recovery rate | 0.7372 yr⁻¹ |
| $\gamma_{22}$ | Diabetic individuals’ resistant TB infection recovery rate | 0.7372 yr⁻¹ |
| $\delta_{1}$ | Rate of death due to TB | 0 yr⁻¹ |
| $\delta_{2}$ | Rate of death due to TB and diabetes | 0 yr⁻¹ |
| $\tau_{1}$ | Modification parameter | 1.01 |
| $\tau_{2}$ | Modification parameter | 1.01 |
| $\Delta_{1}$ | Non-diabetic individuals of partial immunity | 0.0986 yr⁻¹ |
| $\Delta_{11}$ | Non-diabetic individuals’ partial immunity for sensitive recovered | 0.0986 yr⁻¹ |
| $\Delta_{2}$ | Non-diabetic individuals’ partial immunity after resistant recovery | 0.0986 yr⁻¹ |
| $\sigma_{3}$ | Diabetic individuals’ partial immunity | 0.1 yr⁻¹ |
| $\sigma_{31}$ | Sensitive recovered diabetic individuals’ partial immunity | 0.73 P |
| $\sigma_{32}$ | Resistant recovered diabetic individuals’ partial immunity | 0.73 P |
| $\sigma_{33}$ | Sensitive recovered non-diabetic individuals’ degree of immunity | 0.71 P |
| $\sigma_{34}$ | Resistant recovered non-diabetic individuals’ degree of immunity | 0.71 P |
| $\sigma_{35}$ | Sensitive recovered diabetic individuals’ degree of immunity | 0.71 P |
| $\sigma_{36}$ | Recovered diabetic individuals’ degree of immunity | 0.71 P |
optimal controls. Then, there exists co-state variables satisfying the following:

\[ D_t^0 S_1 = \frac{\partial h_a}{\partial \lambda_1} \]

Moreover,

\[ D_t^R = \frac{\partial h_a}{\partial \lambda_1} \]

Moreover, \( \lambda_i(T_f) = 0 \), \( \lambda_1, \lambda_2, \ldots, \lambda_{14} \). (23)

are the Lagrange multipliers. Eqs. (21) and (22) describe the necessary conditions in terms of a Hamiltonian for the optimal control problem defined above. We arrive at the following theorem:

**Theorem 2.** Let \( S_i, E_{1i}, E_{2i}, E_{1R}, E_{2R}, E_{1R}, E_{2R}, \ldots \) be the solutions of the state system and \( u_i, i = 1, \ldots, 4 \) be the given optimal controls. Then, there exists co-state variables \( \lambda_i, j = 1, \ldots, 14 \) satisfying the following:

(1) Co-state equations:

\[ D_t^\lambda \lambda_1 = \left( \left( -\lambda_2^2 + \lambda_2 - \lambda_3 \right) \lambda_1 + \lambda_2^3 \lambda_2 + \left( \lambda_3 + \lambda_2 - \lambda_3 \lambda_2 \right) \right) + \left( \lambda_1 \lambda_2 \lambda_3 \right) \lambda_2 + \left( \lambda_2 \lambda_2 \lambda_3 \right) \lambda_2 \]

\[ D_t^\lambda \lambda_2 = \left( \left( -\lambda_2^2 + \lambda_2 - \lambda_3 \right) \lambda_2 + \left( \lambda_3 + \lambda_2 - \lambda_3 \lambda_2 \right) \right) + \left( \lambda_1 \lambda_2 \lambda_3 \right) \lambda_2 + \left( \lambda_2 \lambda_2 \lambda_3 \right) \lambda_2 \]

\[ D_t^\lambda \lambda_3 = \left( \left( -\lambda_2^2 + \lambda_2 - \lambda_3 \right) \lambda_2 + \left( \lambda_3 + \lambda_2 - \lambda_3 \lambda_2 \right) \right) + \left( \lambda_1 \lambda_2 \lambda_3 \right) \lambda_2 + \left( \lambda_2 \lambda_2 \lambda_3 \right) \lambda_2 \]

\[ D_t^\lambda \lambda_4 = \left( \left( -\lambda_2^2 + \lambda_2 - \lambda_3 \right) \lambda_2 + \left( \lambda_3 + \lambda_2 - \lambda_3 \lambda_2 \right) \right) + \left( \lambda_1 \lambda_2 \lambda_3 \right) \lambda_2 + \left( \lambda_2 \lambda_2 \lambda_3 \right) \lambda_2 \]

\[ D_t^\lambda \lambda_5 = \left( \left( -\lambda_2^2 + \lambda_2 - \lambda_3 \right) \lambda_2 + \left( \lambda_3 + \lambda_2 - \lambda_3 \lambda_2 \right) \right) + \left( \lambda_1 \lambda_2 \lambda_3 \right) \lambda_2 + \left( \lambda_2 \lambda_2 \lambda_3 \right) \lambda_2 \]

(30)
\[ 1 + (1 - P_2) \beta_{21} S_2 z_1' + \beta_{21} \xi_1' \sigma_{21} - (1 - r_2') \sigma_1 \beta_{12} E_{2j} z_1' + \]

\[ (1 - \xi) P_1 \beta_{21} S_3 z_1' + (1 - r_2') \sigma_1 \beta_{12} E_{3j} z_1' + \xi P_1 \beta_{21} S_3 z_1' + \]

\[ (1 - r_2') \beta_{21} E_{2j} z_1' \sigma_1 + (1 - \xi) P_2 \beta_{21} S_2 z_2' + \xi P_2 \beta_{21} S_2 z_2' + \]

\[ + (\eta_2' \xi + \gamma_2' + \mu r + d_2' + \omega_2 u_2(t) \xi)' z_2' + (1 - r_2') \sigma_2 \beta_{21} E_{2j} z_1' + \]

\[ + (1 - r_2') \sigma_2 \beta_{21} E_{2j} z_1' + \xi \beta_{21} S_2 z_3' + \]

\[ \sigma_{31} (1 - \delta_1') \beta_{21} R_{1j} z_1' + \sigma_{32} (1 - \delta_2') \beta_{21} R_{2j} z_1' + \]

\[ + \beta_{21} E_{1j} \xi_1' + \xi P_1 \beta_{21} S_3 z_1' + (1 - r_2') \beta_{21} E_{1j} \xi_1' + \xi P_1 \beta_{21} S_3 z_1' + \]

\[ + (1 - \xi) (1 - P_2) \beta_{21} S_2 z_2' + \xi P_2 \beta_{21} S_2 z_2' + \]

\[ + (1 - r_2') \sigma_2 \beta_{21} E_{2j} z_1' + \xi \beta_{21} S_2 z_3' + \]

\[ (1 - \xi) P_3 \beta_{21} S_3 z_1' + (1 - r_2') \sigma_3 \beta_{21} E_{3j} z_1' + \xi P_3 \beta_{21} S_3 z_1' + \]

\[ + \beta_{21} R_{1j} z_1' \sigma_1 + (\gamma_2' + \mu r + d_2' + \omega_2 u_2(t) \xi)' z_2' + \]

\[ + \sigma_{41} (1 - \delta_1') \beta_{21} R_{1j} z_1' + \sigma_{42} (1 - \delta_2') \beta_{21} R_{2j} z_1' + \]

\[ + \beta_{21} R_{1j} \xi_1' \sigma_1 + (1 - \xi) P_1 \beta_{21} S_3 z_1' + \]

(ii) Transversality conditions:

\[ \xi_j(T_f) = 0, \ j = 1, 2, ..., 14. \]  

(iii) Optimality conditions:

\[ H_u(S_i, S_j, E_1, E_2, E_3, r_1, r_2, r_3, r_4, u_1, u_1, u_2, u_2, \gamma) = \min_{0 < t < T} \{ H(S_i, S_r, E_1, E_2, E_3, r_1, r_2, r_3, r_4, u_1, u_1, u_2, u_2, \gamma) \} \]

\[ u_1' = \min \{ 1 \max \{ 0, \frac{(\omega_2 u_2(t)/(\gamma_{11} - \gamma_{12}))}{B_1} \} \} \]

\[ u_2' = \min \{ 1 \max \{ 0, \frac{(\omega_2 u_2(t)/(\gamma_{12} - \gamma_{11}))}{B_2} \} \} \]

\[ u_3' = \min \{ 1 \max \{ 0, \frac{(\omega_2 u_2(t)/(\gamma_{11} - \gamma_{12}))}{B_3} \} \} \]

\[ u_4' = \min \{ 1 \max \{ 0, \frac{(\omega_2 u_2(t)/(\gamma_{12} - \gamma_{11}))}{B_4} \} \} \]

Proof. We find the co-state system Eqs. (24)-(37), from Eq. (21), where

\[ H_u = \frac{1}{2} u_1^2 + \frac{1}{2} u_2^2 + \frac{1}{2} u_3^2 + \frac{1}{2} u_4^2 \]

\[ + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) \]

\[ + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) \]

\[ + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) \]

\[ + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) \]

\[ + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) \]

\[ + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) \]

\[ + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) + \frac{1}{2} u_2^2(t) \]
\[ a^\alpha \frac{d^p}{dt^p} y(t) = g(t, y(t)), \quad y(0) = y_0. \]  

Applying the fundamental theorem of FC to Eq. (59), we obtain
\[ y(t) - y(0) = \frac{1 - \alpha}{\Gamma(\alpha)} g(t, y(t)) + \frac{\alpha}{\Gamma(\alpha)\Gamma(1-\alpha)} \int_0^t g(\theta, y(\theta))(t - \theta)^{\alpha-1}\,d\theta, \]
where \( \Gamma(x) = 1 - \alpha + \frac{\alpha}{\Gamma(\alpha)} \) is a normalization function, and at \( t_{n+1} \), we have
\[ y_{n+1} - y_0 = \frac{\Gamma(\alpha)(1 - \alpha)}{\Gamma(\alpha)\Gamma(1-\alpha)} g(t_n, y(t_n)) + \frac{\alpha}{\Gamma(\alpha)\Gamma(1-\alpha)} \times \sum_{m=0}^{n} g(t_{n+1} - \theta)^{\alpha-1}\,d\theta. \]

Now, \( g(\theta, y(\theta)) \) will be approximated in an interval \( [t_n, t_{n+1}] \) using a two-step Lagrange interpolation method. The two-step Lagrange polynomial interpolation is given as follows [22]:
\[ P = \frac{g(t_{n+1}, y_{n+1})}{h}(\theta - t_{n+1}) - \frac{g(t_{n+1}, y_{n+1})}{h}(t_n - \theta). \]

Eq. (62), is replaced in Eq. (61), and by performing the same steps in [22], we obtain

\[ a^\alpha \frac{D^p}{dt^p} R_{1R} = \frac{\alpha}{\Gamma(\alpha)\Gamma(1-\alpha)} \int_0^t g(\theta, y(\theta))(t - \theta)^{\alpha-1}\,d\theta, \]
where
\[ B(x) = 1 - \alpha + \frac{\alpha}{\Gamma(\alpha)} \]

is a normalization function, and at \( t_{n+1} \), we have
\[ y_{n+1} - y_0 = \frac{\Gamma(\alpha)(1 - \alpha)}{\Gamma(\alpha)\Gamma(1-\alpha)} g(t_n, y(t_n)) + \frac{\alpha}{\Gamma(\alpha)\Gamma(1-\alpha)} \times \sum_{m=0}^{n} g(t_{n+1} - \theta)^{\alpha-1}\,d\theta. \]

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\[ P = \frac{g(t_{n+1}, y_{n+1})}{h}(\theta - t_{n+1}) - \frac{g(t_{n+1}, y_{n+1})}{h}(t_n - \theta). \]
\[
y_{n+1} - y_0 = \frac{\Gamma(x)(1-x)}{\Gamma(x)(1-x) + x^a g(t_n, y(t_n))} + \frac{1}{(x+1)(1-x)^2} \times \sum_{m=0}^{n} h^a g(t_m, y(t_m))(n+1-m)^a
\]

\[
(n - m + 2 + a) - (n - m)^2(n - m + 2 + 2a)
\]

\[
(n - m + 2 + a) - (n - m)^2(n - m + 1 + a).
\]  

To obtain high stability, we present a simple modification in Eq. (63). This modification is to replace the step size \( h \) with \( \phi(h) \) such that

\[
\phi(h) = h + O(h^2), \quad 0 < \phi(h) \leq 1.
\]

For more details, see [54]. Then, the new scheme is called the nonstandard two-step Lagrange interpolation method (NS2LIM) and is given as follows:

\[
y_{n+1} - y_0 = \frac{\Gamma(x)(1-x)}{\Gamma(x)(1-x) + x^a g(t_n, y(t_n))} + \frac{1}{(x+1)(1-x)^2} \times \sum_{m=0}^{n} \phi(h)^a g(t_m, y(t_m))
\]

\[
(n + 1 - m)^a(n - m + 2 + a) - (n - m)^2(n - m + 2 + 2a)
\]

\[
(n + 1 - m)^a(n - m + 2 + a) - (n - m)^2(n - m + 1 + a).
\]

Then, we use the new scheme in Eq. (64) to numerically solve the state system in Eqs. (45)–(58), and we use the implicit finite difference method to solve the co-state system Eqs. (24)–(37) with the transversality conditions in Eq. (38).

**Numerical simulations**

In this section, we present two new schemes in Eqs. (63) and (64) to numerically simulate the fractional-order optimal system in Eqs. (45)–(58) and Eqs. (24)–(37) with the transversality condition in Eq. (38) using the parameters given in Table 1 and \( \phi(h) = Q(1 - e^{-h}) \), where \( Q \) is a positive number less than or equal to 0.01. The initial conditions are \( S_1(0) = 8741400, S_2(0) = 200000, E_{1i}(0) = 557800, E_{2i}(0) = 7800, E_{1f}(0) = 4500, E_{2f}(0) = 3000, I_{1s}(0) = 20000, I_{2s}(0) = 2000, I_{1e}(0) = 1800, I_{2e}(0) = 800, R_{1i}(0) = 800, R_{2i}(0) = 800, R_{2i}(0) = 200, \) and \( R_{2f}(0) = 100 \). For computational purposes, we use MATLAB on a computer with the 64-bit Windows 7 operating system and 4 GB of RAM. We now show some numerical aspects of the simulation of the proposed model in Eqs. (3)–(16). Fig. 2 shows that the summation of all the unknown of variables in the proposed model in Eqs. (3)–(16) is strictly constant during the studied time in the controlled case when using the scheme in Eq. (64). This result indicates that the proposed method is efficient. Fig. 3 shows the numerical solutions of \( I_{1s}, I_{2s}, I_{1e}, \) and \( I_{2e} \) using the scheme in Eq. (64) when \( T_f = 200 \) in the controlled case. We note that the solutions for different values of \( \alpha \) vary close to the integer-order solution, i.e., the FO model is a generalization of the integer-order model and the FOCP systems and is more suitable for describing the real world. In Figs. 4–6, we examined the numerical results of \( I_{1s}, I_{2s}, I_{1e}, \) and \( I_{2e} \) in the case \( \alpha = 0.95, 1 \), and we note that there are fewer infected individuals

![Fig. 4. Numerical simulations of \( I_{1s}, I_{2s}, I_{1e}, \) and \( I_{2e} \) with \( \alpha = 0.95 \) and \( \beta = 9 \) without control cases using NS2LIM.](image)
in the control case. These results agree with the results given in Table 2. Fig. 7 illustrates the behaviour of relevant variables from the proposed model in Eqs. (3)–(16) for different values of $\alpha$ using the scheme in Eq. (64). We note that the relevant variables change under different values of $\alpha$ following the same behaviour. Fig. 8 shows the behaviours of the relevant variables from the proposed model in Eqs. (3)–(16) for $\alpha = 0.8$ using the scheme in Eq. (63). We note that the relevant variables exhibit the same behaviour. Fig. 9
shows the behaviour of the control variables $u_2$ and $u_3$ at different values of $a$ and $T_f = 200$ using NS2LM. We note that the control variables exhibit the same behaviour in the integer and fractional cases. Fig. 10 shows that the proposed scheme in Eq. (64) is more stable than the scheme in Eq. (63). Table 2 shows a comparison of the value of the objective function system using Eq. (64) with and without control cases when $T_f = 50$ and under different values of $a$. We note that the values of the objective function system with the control cases are lower than the values of the objective function system without the controls for all values of $0.6 < \alpha \leq 1$.

### Table 2
Comparison of the values of the objective function system using NS2LM and $T_f = 50$ with and without control cases.

| $\alpha$ | $J(u_1, u_2, u_3)$ with control | $J(u_1, u_2, u_3)$ without controls |
|---------|---------------------------------|-------------------------------------|
| 1       | $8.7371 \times 10^5$            | $1.0721 \times 10^5$               |
| 0.98    | $8.6240 \times 10^5$            | $1.0581 \times 10^5$               |
| 0.95    | $8.4617 \times 10^5$            | $1.0383 \times 10^5$               |
| 0.90    | $8.2138 \times 10^5$            | $1.0082 \times 10^5$               |
| 0.80    | $7.8340 \times 10^5$            | $9.6373 \times 10^5$               |
| 0.75    | $7.7330 \times 10^5$            | $9.5414 \times 10^5$               |
| 0.60    | $8.2733 \times 10^5$            | $1.0502 \times 10^5$               |

Table 3 shows a comparison of the two proposed schemes in Eqs. (64) and (63) under different values of $\alpha$ with the control case. The solutions for the scheme in Eq. (64) appear to be slightly more accurate than those for the scheme in Eq. (63).

### Conclusions
In this article, an optimal control for a fractional TB infection model that includes the impact of diabetes and resistant strains is presented. The fractional derivative is defined in the ABC sense. The proposed mathematical model utilizes a non-local and non-singular kernel. Four optimal control variables, $u_1$, $u_2$, $u_3$, and $u_4$, are introduced to reduce the number of individuals infected. It is concluded that the proposed fraction-order model can potentially describe more complex dynamics than can the integer model and can easily include the memory effects present in many real-world phenomena. Two numerical schemes are used: 2LIM and NS2LIM. Some figures are given to demonstrate how the fractional-order model is a generalization of the integer-order model. Moreover, we numerically compare the two methods. It is found that NS2LIM is more accurate, more efficient, more direct and more stable than 2LIM.
Fig. 8. Dynamics of relevant variables of the system in Eqs. (45)–(58) when $B_1 = B_2 = B_3 = B_4 = 100$ and $\beta = 5$, with control cases using 2LIM.

Fig. 9. Numerical simulations of the control variables using NS2LIM.
Compliance with Ethics Requirements

This article does not contain any studies with human or animal subjects.

Conflict of interest

The authors have declared no conflict of interest.

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Table 3

Comparison of 2LIM and NS2LIM in the controlled case with $T_f = 10$, $h = 0.1$ and $\beta = 5$

| Variables | 2LIM | NS2LIM | $x$ |
|-----------|------|--------|-----|
| $l_{1R}$  | $6.0500 \times 10^3$ | $1.9694 \times 10^3$ | 0.8 |
| $l_{2s}$  | $1.7822 \times 10^3$ | $1.5554 \times 10^3$ | 0.7 |
| $l_{1R}$  | $4.0922 \times 10^3$ | $1.9382 \times 10^3$ | 0.6 |
| $l_{2s}$  | $3.1513 \times 10^3$ | $1.6662 \times 10^3$ | 0.6 |
| $l_{1R}$  | $2.9203 \times 10^3$ | $1.9168 \times 10^3$ | 0.6 |
| $l_{2s}$  | $6.2351 \times 10^3$ | $2.3815 \times 10^3$ | 0.6 |

Fig. 10. Numerical simulations of $R_t$ when $B_1 = B_2 = B_3 = B_4 = 100$ and $x = 0.9$, $h = 1$ with control case using NS2LIM and 2LIM.
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