Journal of Mathematical Modeling and Fractional Calculus
https://acspublisher.com/journals/index.php/jmmfc
Received:20-02-2024, **Revised:** 16-03-2024,
Accepted:10-04-2024, **Published:** ,
DOI: 1(1),78-88.

Analyzing the Dynamics of Tuberculosis through a Fractional-Order Model

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Abstract: Tuberculosis (TB) remains a significant public health challenge worldwide, exacerbated by the complex and persistent nature of Mycobacterium tuberculosis infection. Traditional integer-order models provide insight into TB transmission and control but may fall short in capturing the nuances of disease progression and memory effects inherent in biological systems. This study presents a fractional-order mathematical model of TB dynamics to better reflect the complexities of TB infection, latency, and progression. Utilizing fractional calculus, the model introduces a novel approach that accounts for memory and hereditary properties, offering a more accurate representation of disease transmission and latency. Analytical methods are applied to explore the behavior of the disease dynamics. Numerical simulations validate the model's effectiveness in describing TB dynamics. The fractional-order TB model has the potential to inform more effective intervention strategies and improve predictions of long-term outcomes.

Keywords: Drinking Model; Tuberculosis, Fractional-order model, Mathematical Modeling, Numerical Analysis.

1. Introduction

Tuberculosis (TB), caused by the bacterium Mycobacterium tuberculosis, remains one of the leading causes of infectious disease mortality worldwide [1, 2, 3]. Despite global efforts to reduce its incidence, TB continues to pose a public health burden, particularly in low- and middle-income countries [4, 5]. Traditional mathematical models have played a critical role in understanding TB dynamics, informing policymakers, and aiding in the design of effective control strategies [6, 7]. However, many of these models rely on integer-order derivatives, which, while useful, may not fully capture the complex dynamics of TB infection and progression. Biological systems often exhibit memory and hereditary characteristics, particularly in the case of chronic infectious diseases like TB, where the latency period and immune response play essential roles in disease spread and control. Fractional calculus, which extends traditional integer-order differentiation to non-integer orders, provides a more flexible framework to model these memory effects. Fractional-order models have shown promise in various fields of epidemiology by capturing the long-term dependencies and memory effects observed in disease dynamics [8, 9, 10, 11, 12, 13, 14, 15]. In this study, we develop a fractional-order TB model that integrates these unique properties, offering a more nuanced view of TB dynamics. This model distinguishes itself by incorporating fractional-order derivatives to simulate the latency and progression of TB in a population more realistically. By extending classical models with fractional calculus, we aim to explore how fractional orders can provide new insights into TB transmission and persistence. Through a combination of theoretical analysis and numerical simulations, this study seeks to illustrate

the advantages of fractional-order modeling in capturing TB dynamics under various epidemiological conditions. By examining how different fractional orders influence disease progression and latency, our approach provides an adaptable framework for understanding TB and other complex infectious diseases. This work contributes to the expanding field of fractional epidemiological modeling and opens pathways for further research into the applications of fractional calculus in public health.

2. Preliminaries

In this section, we introduce certain definitions and properties of fractional integrals and derivatives, which will be utilized subsequently.

definition 1 Let $\alpha \in \mathbb{R}$, $n-1 < \alpha \leq n$, $n \in \mathbb{N}$, and $f(t)$ an absolutely continuous function on the interval $[0,\infty)$. The Caputo fractional derivative of order α is defined as follows [16, 17]:

$$ {}_0^c D_t^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \int_0^t \underbrace{(t-s)^{n-\alpha-1} f^{(n)}(s)}_{\text{Kernel and higher-order derivative of } f(t)} ds, \quad t \in [0,T_f],\ \alpha \in (0,1], $$

where $f(t)$ is an n-times differentiable function, and $\Gamma(x)$ is the Gamma function:

$$ \Gamma(x) = \int_0^\infty \underbrace{e^{-z} z^{x-1}}_{\text{decaying exponential and power function}} dz, \quad \mathrm{Re}(z) > 0. $$

definition 2 The Riemann–Liouville fractional integral of order $\alpha > 0$ for a function $f(t)$ is defined by [16, 17]:

$$ {}_0^{RL} I_t^\alpha f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t \underbrace{(t-s)^{\alpha-1} g(s)}_{\text{Kernel function and } f(t)} ds, \quad t \in [0,T_f], $$

which exists almost everywhere for any integrable function $f(t)$.

The Riemann–Liouville integral and the Caputo fractional derivative operators satisfy the following key property:

$$ {}_0^{RL} I_t^\alpha \left({}_0^c D_t^\alpha f(t)\right) = f(t) - \sum_{k=0}^{n-1} \underbrace{f^{(k)}(0)\frac{t^k}{k!}}_{\text{Polynomial of lower-order terms}}, \quad n-1 < \alpha \leq n. $$

definition 3 The Mittag–Leffler functions, which play a significant role in fractional calculus, are defined as follows:

$$ E_\sigma(w) = \sum_{k=0}^{\infty} \frac{w^k}{\Gamma(1+k\sigma)}, \quad \sigma \in \mathbb{C},\ \mathrm{Re}(\sigma) > 0,\ w \in \mathbb{C}, $$

and its generalized form

$$ E_{\sigma,\varsigma}(w) = \sum_{k=0}^{\infty} \frac{w^k}{\Gamma(\varsigma+k\sigma)}, \quad \sigma,\varsigma \in \mathbb{C},\ \mathrm{Re}(\sigma),\mathrm{Re}(\varsigma) > 0,\ w \in \mathbb{C}, $$

are called the generalized Mittag–Leffler functions [18].

Symbol	Description	Type
$\mathscr{S}(t)$	Susceptible individuals at time t	Variable
$\mathscr{A}(t)$	Asymptomatic (Latent TB) individuals at time t	Variable
$\mathscr{C}(t)$	Symptomatic (Active TB) individuals at time t	Variable
$\mathscr{T}(t)$	Individuals under TB treatment at time t	Variable
$\mathscr{R}(t)$	Recovered individuals (after successful treatment) at time t	Variable
$\mathscr{N}(t)$	Total population at time t	Variable
$\mathscr{M}^{\alpha}$	Recruitment rate of susceptible individuals	Parameter
$\mathfrak{b}^{\alpha}$	Rate of transmission of TB from symptomatic to susceptible	Parameter
μ^{α}	Natural death rate (applies to all compartments)	Parameter
$\mathfrak{r}^{\alpha}$	Rate of reactivation of latent TB to active TB	Parameter
δ^{α}	Rate at which active TB individuals are treated	Parameter
σ^{α}	Rate of recovery for individuals under treatment	Parameter
γ^{α}	Recovery rate of treated individuals moving to recovered class	Parameter
$\mathfrak{d}^{\alpha}$	Death rate due to TB for symptomatic individuals	Parameter

Table 1: Variables and Parameters for the Fractional-Order Tuberculosis (TB) Model

3. Model Formation

The fractional-order Tuberculosis system of equations is given by:

$$\begin{cases} \mathscr{D}_t^{\alpha}\mathscr{S}(t) = \mathscr{M}^{\alpha} + \mathfrak{r}^{\alpha}\mathscr{R}(t) - \dfrac{\mathfrak{b}^{\alpha}\mathscr{S}(t)}{\mathscr{N}(t)}\mathscr{A}(t) - \mu^{\alpha}\mathscr{S}(t), \\ \mathscr{D}_t^{\alpha}\mathscr{A}(t) = \dfrac{\mathfrak{b}^{\alpha}\mathscr{S}(t)}{\mathscr{N}(t)}\mathscr{A}(t) - \mu^{\alpha}\mathscr{A}(t) - \delta^{\alpha}\mathscr{A}(t)\mathscr{C}(t), \\ \mathscr{D}_t^{\alpha}\mathscr{C}(t) = \delta^{\alpha}\mathscr{A}(t)\mathscr{C}(t) - \mu^{\alpha}\mathscr{C}(t) - \sigma^{\alpha}\mathscr{C}(t) - \mathfrak{d}^{\alpha}\mathscr{C}(t), \\ \mathscr{D}_t^{\alpha}\mathscr{T}(t) = \sigma^{\alpha}\mathscr{C}(t) - \gamma^{\alpha}\mathscr{T}(t) - \mu^{\alpha}\mathscr{T}(t), \\ \mathscr{D}_t^{\alpha}\mathscr{R}(t) = \gamma^{\alpha}\mathscr{T}(t) - \mu^{\alpha}\mathscr{R}(t) - \mathfrak{r}^{\alpha}\mathscr{R}(t), \end{cases} \tag{1}$$

where

$$\mathscr{S}(t) + \mathscr{A}(t) + \mathscr{C}(t) + \mathscr{T}(t) + \mathscr{R}(t) = \mathscr{N}(t), \quad 0 < \alpha < 1.$$

4. Analysis of the Model

Theorem 1 The fractional-order system in (1) possesses a unique, bounded solution.

Proof. We begin by analyzing the total derivative of the system (1):

$$\begin{cases} \mathscr{D}_t^{\alpha}\mathscr{N}(t) = \mathscr{M}^{\alpha} - \mu^{\alpha}(\mathscr{S}(t) + \mathscr{A}(t) + \mathscr{C}(t) + \mathscr{T}(t) + \mathscr{R}(t)) - \mathfrak{d}^{\alpha}\mathscr{C}(t), \\ \qquad\qquad = \mathscr{M}^{\alpha} - \mu^{\alpha}\mathscr{N}(t) - \mathfrak{d}^{\alpha}\mathscr{C}(t). \end{cases}$$

Applying Grnwalls inequality with the initial condition $\mathscr{N}(t_0) \geq 0$, and taking the Laplace transform $\mathscr{L}\{\cdot\}$ on both sides, we obtain:

$$\mathscr{L}\left\{\mathscr{D}_t^{\alpha}\mathscr{N}(t) + \mu^{\alpha}\mathscr{N}(t)\right\} \leq \mathscr{L}\left\{\mathscr{M}^{\alpha}\right\}.$$

This results in the following in terms of the Laplace variable s:

$$\begin{cases} \mathscr{L}\{\mathscr{N}(t)\}(s^\alpha+\mu^\alpha) \leq \sum_{m=0}^{n-1} s^{\alpha-m-1}\mathscr{N}^{(m)}(t_0) + \dfrac{\mathscr{M}^\alpha}{s(s^\alpha+\mu^\alpha)}, \\ \mathscr{L}\{\mathscr{N}(t)\} \leq \sum_{m=0}^{n-1} \dfrac{s^{\alpha-m-1}}{s^\alpha+\mu^\alpha}\mathscr{N}^{(m)}(t_0) + \dfrac{\mathscr{M}^\alpha}{s(s^\alpha+\mu^\alpha)}. \end{cases}$$

Using partial fractions, we expand as follows:

$$\mathscr{L}\{\mathscr{N}(t)\} \leq \mathscr{M}^\alpha\mu^\alpha\left[\frac{1}{s} - \frac{1}{s\left(1+\frac{\mu^\alpha}{s^\alpha}\right)}\right] + \sum_{m=0}^{n-1}\frac{1}{s^{m+1}\left(1+\frac{\mu^\alpha}{s^\alpha}\right)}\mathscr{N}^{(m)}(t_0).$$

Next, apply the Taylor expansion:

$$\mathscr{L}\{\mathscr{N}(t)\} \leq \mathscr{M}^\alpha\mu^\alpha\left[\frac{1}{s} - \frac{1}{s}\sum_{n=0}^{\infty}\left(-\frac{\mu^\alpha}{s^\alpha}\right)^n\right] + \sum_{m=0}^{n-1}\sum_{n=0}^{\infty}\left(-\frac{\mu^\alpha}{s^\alpha}\right)^n\frac{\mathscr{N}^{(m)}(t_0)}{s^{\alpha n+m+1}}.$$

Now, to express the solution, we introduce the Mittag-Leffler function from Definition 2:

$$E_{\alpha,\beta}(z) = \sum_{k=0}^{\infty}\frac{z^k}{\Gamma(\alpha k+\beta)}, \quad \alpha>0,\ \beta>0.$$

Hence, the inverse Laplace transform gives:

$$\mathscr{N}(t) \leq \mathscr{M}^\alpha\mu^\alpha\left[1-E_\alpha\left(-\mu^\alpha t^\alpha\right)\right] + \sum_{m=0}^{n-1}E_{\alpha,m+1}\left(-\mu^\alpha t^\alpha\right)\mathscr{N}^{(m)}(t_0)t^m.$$

Since the series of Mittag-Leffler functions $E_\alpha(-\mu^\alpha t^\alpha)$ and $E_{\alpha,m+1}(-\mu^\alpha t^\alpha)$ converge, $\mathscr{N}(t)$ is bounded.

Next, we express each equation of the system in the general form:

$$\mathscr{D}_t^\alpha\mathscr{Y}(t) = \mathscr{G}(t,\mathscr{Y}), \quad \mathscr{Y}(0) = \mathscr{Y}_0.$$

To prove uniqueness, we check the Lipschitz continuity of $\mathscr{G}$:

$$|\mathscr{G}(t,\mathscr{Y}) - \mathscr{G}(t,\mathscr{Y}^*)| = |P(\mathscr{Y}) + Q(\mathscr{Y}) + r - (P(\mathscr{Y}^*) + Q(\mathscr{Y}^*) + r)| \leq M\|\mathscr{Y}-\mathscr{Y}^*\|.$$

Here, $\mathscr{M} = (|P|+1)$ and $\mathscr{M}|\mathscr{Y}(t)-\mathscr{Y}^*(t)| < \infty$.
Since $\mathscr{G}$ is Lipschitz continuous and bounded, we apply the Banach fixed-point theorem to confirm that the system admits a unique solution. Using the Picard-Lindelf theorem, we conclude that the system has a unique, bounded solution in the biologically feasible domain:

$$\Omega = \left\{(\mathscr{S}(t),\mathscr{A}(t),\mathscr{C}(t),\mathscr{T}(t),\mathscr{R}(t)) \in \mathbb{R}^5 \mid \mathscr{N}(t) \leq \frac{\mathscr{M}^\alpha}{\mu^\alpha}\left[1-E_\alpha\left(-\mu^\alpha t^\alpha\right)\right]\right\}.$$

□

5. Numerical Analysis

In this section, we present the numerical scheme used to solve the fractional-order tuberculosis (TB) model introduced in (1). The system of fractional differential equations (FDEs) is solved using the predictor-corrector PECE (Predict-Evaluate-Correct-Evaluate) scheme of the AdamsBashforthMoulton type. This method is chosen for its efficiency in handling the non-local memory effects associated

with fractional derivatives. The scheme provides a balance between accuracy and computational complexity, making it well-suited for simulating the dynamics of infectious diseases like TB. We begin by considering a general fractional differential equation (FDE) of the form:

$$ {}_0^C D_t^\alpha Y(t) = f(t, Y(t)), \tag{2} $$

where ${}_0^C D_t^\alpha$ denotes the Caputo fractional derivative, $0 < \alpha < 1$, and $Y(t)$ is the state variable to be solved over a time interval $[t_0, t_f]$. The numerical solution of this equation is obtained using a constant step size h, and the fractional derivative is discretized using the AdamsBashforthMoulton method.

5.1. Predictor-Corrector Method Applied to the TB Model

The fractional derivatives are interpreted in the Caputo sense, and the predictor-corrector method is applied to each equation.
Let h be the step size, $t_n = nh$, and let $\mathscr{Y}_n = \mathscr{Y}(t_n)$ denote the numerical approximation at step n, for $\mathscr{Y} \in \{\mathscr{S}, \mathscr{A}, \mathscr{C}, \mathscr{T}, \mathscr{R}\}$.

Predictor Step:
For each variable $\mathscr{Y}(t)$, the Adams-Bashforth predictor formula at t_{n+1} is given by:

$$ \mathscr{Y}_{\text{pred}}(t_{n+1}) = \mathscr{Y}(t_0) + \frac{h^\alpha}{\Gamma(\alpha+1)} \left(\sum_{j=0}^{n} b_{n-j} f_j(\mathscr{S}, \mathscr{A}, \mathscr{C}, \mathscr{T}, \mathscr{R}) \right), \tag{3} $$

where $f_j(\mathscr{S}, \mathscr{A}, \mathscr{C}, \mathscr{T}, \mathscr{R})$ represents the right-hand side of the corresponding equation for $\mathscr{Y}$ evaluated at t_j, and b_{n-j} are coefficients based on the fractional order α.
For the TB model (1), this translates to:

$$ \begin{cases} \mathscr{S}_{\text{pred}}(t_{n+1}) = \mathscr{S}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+1)} \left(\displaystyle\sum_{j=0}^{n} b_{n-j} \left(\mathscr{M}^\alpha + \mathfrak{r}^\alpha \mathscr{R}_j - \frac{\mathfrak{b}^\alpha \mathscr{S}_j}{\mathscr{N}_j} \mathscr{A}_j - \mu^\alpha \mathscr{S}_j \right) \right), \\ \mathscr{A}_{\text{pred}}(t_{n+1}) = \mathscr{A}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+1)} \left(\displaystyle\sum_{j=0}^{n} b_{n-j} \left(\frac{\mathfrak{b}^\alpha \mathscr{S}_j}{\mathscr{N}_j} \mathscr{A}_j - \mu^\alpha \mathscr{A}_j - \delta^\alpha \mathscr{A}_j \mathscr{C}_j \right) \right), \\ \mathscr{C}_{\text{pred}}(t_{n+1}) = \mathscr{C}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+1)} \left(\displaystyle\sum_{j=0}^{n} b_{n-j} \left(\delta^\alpha \mathscr{A}_j \mathscr{C}_j - \mu^\alpha \mathscr{C}_j - \sigma^\alpha \mathscr{C}_j - \mathfrak{d}^\alpha \mathscr{C}_j \right) \right), \\ \mathscr{T}_{\text{pred}}(t_{n+1}) = \mathscr{T}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+1)} \left(\displaystyle\sum_{j=0}^{n} b_{n-j} \left(\sigma^\alpha \mathscr{C}_j - \gamma^\alpha \mathscr{T}_j - \mu^\alpha \mathscr{T}_j \right) \right), \\ \mathscr{R}_{\text{pred}}(t_{n+1}) = \mathscr{R}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+1)} \left(\displaystyle\sum_{j=0}^{n} b_{n-j} \left(\gamma^\alpha \mathscr{T}_j - \mu^\alpha \mathscr{R}_j - \mathfrak{r}^\alpha \mathscr{R}_j \right) \right). \end{cases} \tag{4} $$

Corrector Step:
The corrector formula refines the predictor using the Adams-Moulton method:

$$ \mathscr{Y}(t_{n+1}) = \mathscr{Y}(t_0) + \frac{h^\alpha}{\Gamma(\alpha+2)} \left(f_0 + \sum_{j=1}^{n} a_{n-j+1} f_j + f_{n+1,\text{pred}} \right), \tag{5} $$

where $f_{n+1,\text{pred}}$ is the value of the right-hand side evaluated at the predicted values.

For the TB model (1):

$$\begin{cases} \mathscr{S}(t_{n+1}) = \mathscr{S}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+2)}\left(f_0 + \displaystyle\sum_{j=1}^{n} a_{n-j+1} f_j + f_{n+1,\text{pred}}\right), \\ \mathscr{A}(t_{n+1}) = \mathscr{A}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+2)}\left(f_0 + \displaystyle\sum_{j=1}^{n} a_{n-j+1} f_j + f_{n+1,\text{pred}}\right), \\ \mathscr{C}(t_{n+1}) = \mathscr{C}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+2)}\left(f_0 + \displaystyle\sum_{j=1}^{n} a_{n-j+1} f_j + f_{n+1,\text{pred}}\right), \\ \mathscr{T}(t_{n+1}) = \mathscr{T}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+2)}\left(f_0 + \displaystyle\sum_{j=1}^{n} a_{n-j+1} f_j + f_{n+1,\text{pred}}\right), \\ \mathscr{R}(t_{n+1}) = \mathscr{R}(t_0) + \dfrac{h^\alpha}{\Gamma(\alpha+2)}\left(f_0 + \displaystyle\sum_{j=1}^{n} a_{n-j+1} f_j + f_{n+1,\text{pred}}\right). \end{cases} \tag{6}$$

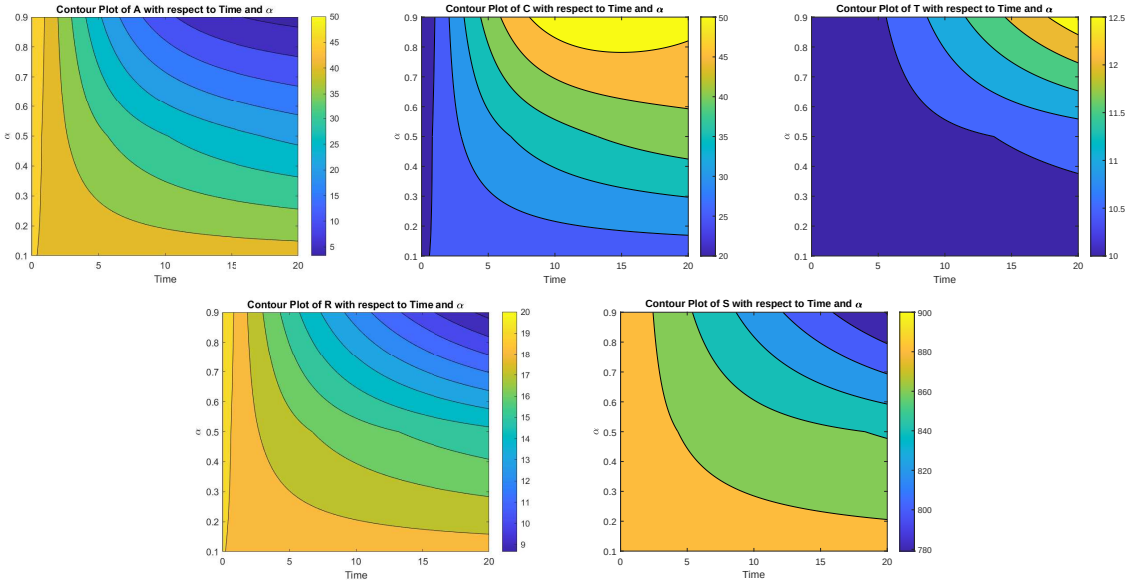

Figure 1: Contour plot of system (1) for $0 < \alpha < 1$.

6. Conclusion

In this study, we developed and analyzed a fractional-order mathematical model for tuberculosis dynamics, incorporating the Caputo derivative to capture memory effects and long-term influences on the progression of the disease. The model accounted for five distinct compartments representing the susceptible, asymptomatic, symptomatic, treated, and recovered populations. By varying the fractional order, we demonstrated how the rate of disease spread, treatment, and recovery can change under time and influence of α as seen through Figures 1, 2 and 3. Our results showed that fractional calculus provides a flexible and powerful framework for studying the transmission dynamics of infectious diseases like TB, allowing for more realistic and dynamic modeling compared to integer-order systems. The simulations revealed key insights into how the disease propagates in a population, with notable interactions between the asymptomatic and symptomatic compartments. The fractional-order approach enabled us to model the slower spread and progression of the disease, as well as the effects of treatment and recovery. The sensitivity of the system to changes in the fractional order highlights the importance of considering non-integer dynamics in real-world epidemiological modeling. This study emphasizes

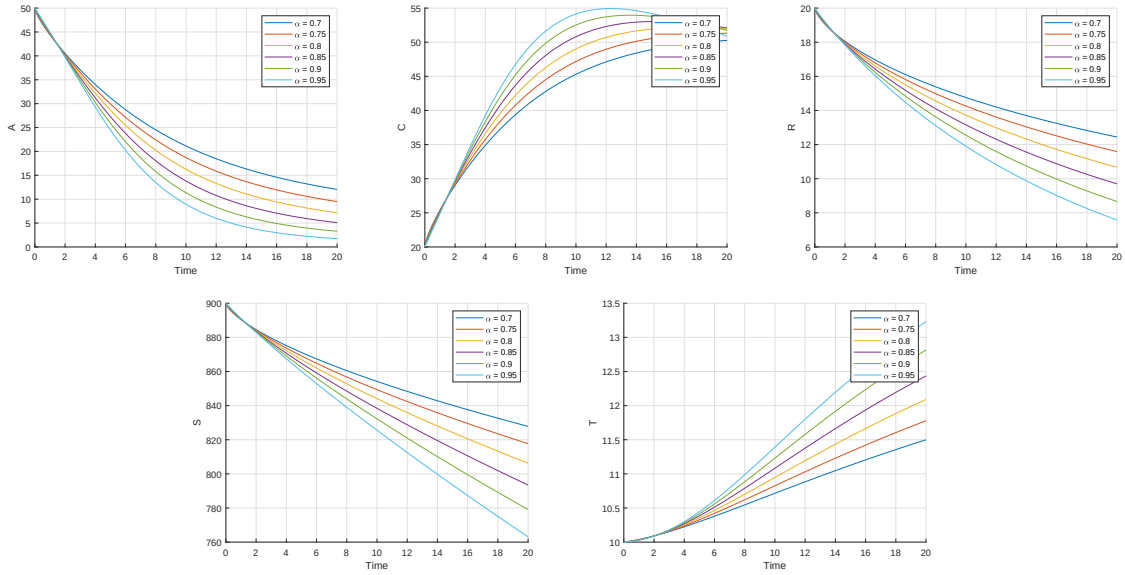

Figure 2: Two dimensional plot of system (1) for α values: $0.7, 0.75, 0.8, 0.85, 0.9, 0.95$.

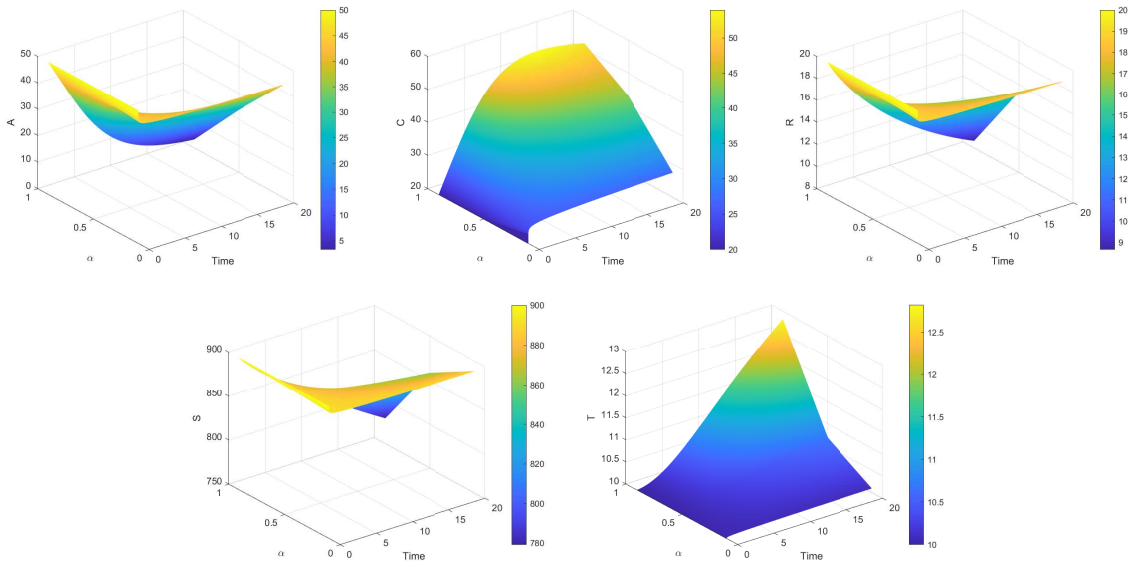

Figure 3: Three dimensional plot of system (1) for $0 < \alpha < 1$.

the importance of fractional-order models in epidemiology, particularly for diseases like TB, where traditional models may not fully capture the complexity of disease progression. Future research could explore the incorporation of additional factors such as optimization control, drug resistance, and co-infections, further enhancing the applicability of fractional calculus in public health modeling and decision-making.

7. Data Availability Statement

All data used are cited within this article.

8. Competing interests

The author declare that they have no competing interests.

9. Funding

Not applicable.

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