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A FRACTIONAL ORDER MODEL FOR THE DYNAMICS OF TUBERCULOSIS SPREAD

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Abstract. In this paper, we establish a mathematical model for Tuberculosis (TB) spread in a human population. The proposed mathematical model is in the form of a nonlinear fractional order differential equation system which is an extension of the *SEIR* epidemic model. The model is constructed based on grouping the population into five compartments, namely the susceptible sub-population compartment, the exposed sub-population compartment, the infected sub-population compartment, the quarantine sub-population compartment, and the recovered sub-population compartment. It was shown that the stability of the equilibrium points of the model depends on the basic reproduction number, and the addition of the quarantine sub-population compartment decreases the number of basic reproduction. A numerical simulation is given to demonstrate the validity of the results. The analysis reveals that the convergence to the equilibrium points becomes faster as the fractional order increases.

Keywords: fractional-order derivative; SEIQR model; basic reproduction number; equilibrium.

2020 AMS Subject Classification: 49L20, 92D25.

1. INTRODUCTION

Tuberculosis (TB) is one infectious illness that is the root cause of a lot of problems. It is typically caused by *Mycobacterium tuberculosis* and affects the lungs. The most typical way

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that someone with irresistible pneumonic TB communicates the disease to others is through bead cores, which are aerosolized by hacking, sniffing, or talking. Despite several decades of study, the widespread availability of a vaccine, and a clear WHO drive to support a coordinated worldwide TB control plan, tuberculosis remains a major cause of infectious disease-related mortality [1, 2].

The transmission of tuberculosis (TB) disease has been studied by many researchers using mathematical models in the form of nonlinear differential equations, as seen in [3, 6, 5, 4, 7]. It has been shown that mathematical modeling is important for better understanding the dynamics of tuberculosis transmission as well as for evaluating the effectiveness of various control and prevention strategies.

One of the much-explored models of tuberculosis transmission in the form of non-linear differential equations is the *SEIR* model, see [3, 8, 9]. In their model, the observed human population at time t , denoted by $N(t)$, is divided into fourth epidemiological sub-compartments, that are susceptible $S(t)$, exposed during the latent period $E(t)$, TB active (infected) $I(t)$, recovery due to the effective treatment $R(t)$. In general, a basic compartment diagram for *SEIR* model is given in the Figure 1 [3], where the parameter Λ denotes the net inflow of the susceptible population per unit value of time (comprising new births and new residents), d_1 is the natural death rate, α is the contact rate between susceptible and infected, r is the outflow rate from exposed to infected, and σ_2 is the recovery rate due to the effective treatment.

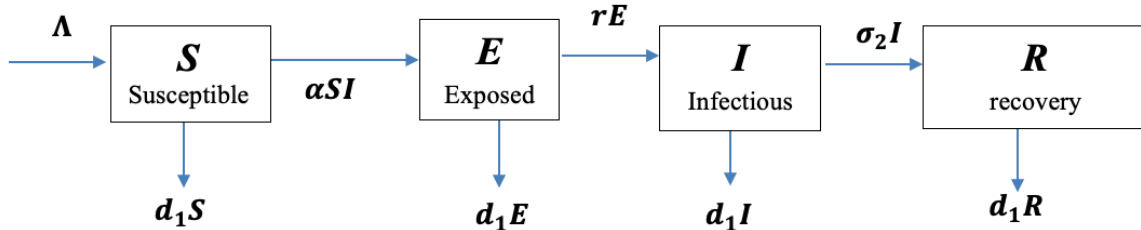


FIGURE 1. Basic compartment diagram of *SEIR* model

Based on the Figure 1, the transmission model for TB dynamics *SEIR* is given by the following system of non-linear differential equations [8, 9]:

$$\begin{aligned}
 \mathcal{D}S &= \Lambda - \alpha SI - d_1 S \\
 \mathcal{D}E &= \alpha SI - (r + d_1) E \\
 \mathcal{D}I &= rE - (d_1 + \sigma_2) I \\
 \mathcal{D}R &= \sigma_2 I - d_1 R,
 \end{aligned}
 \tag{1}$$

where $\mathcal{D} = \frac{d}{dt}$, and the initial conditions

$$S(0) = S_0, E(0) = E_0, I(0) = I_0, R(0) = R_0.
 \tag{2}$$

In this paper, we modify these existing *SEIR* models by adding a compartment quarantine, denoted *Q*, as an effort to prevent the transmission of TB. Figure 2 below illustrates the addition of the quarantine compartment from Figure 1 above, where β_1 is the outflow rate from *E* to *Q*, β_2 is the outflow rate from *I* to *Q*, d_2 is the TB disease-induced death rate, σ_3 is the outflow rate from *E* to *R*, and τ is the outflow rate from *R* to *S*.

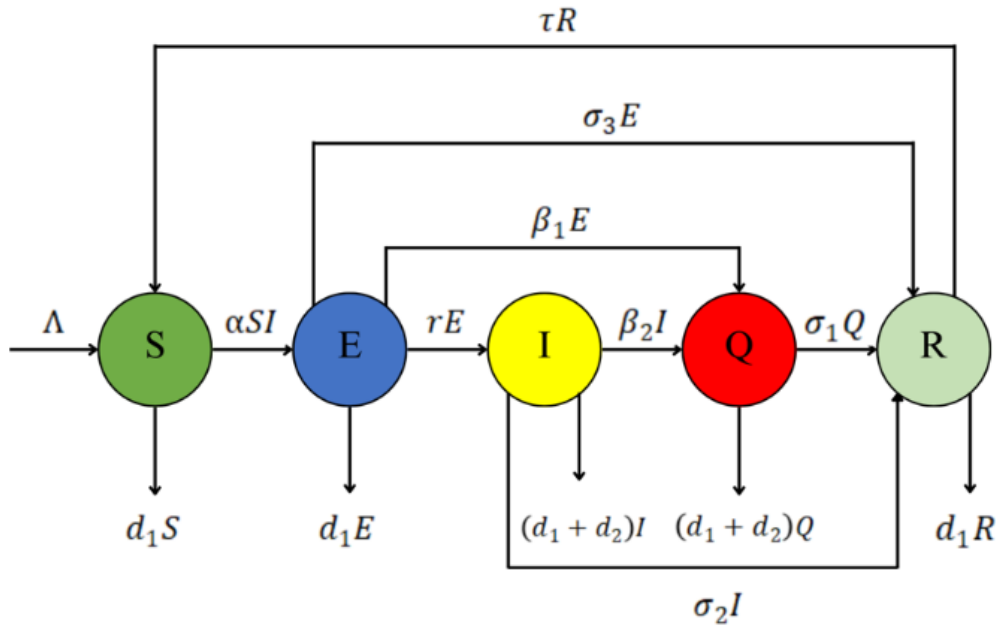


FIGURE 2. Compartment diagram of *SEIQR* model

In addition, in this paper, we use the fractional derivative of Caputo type as a replacement the usual derivative. It is well known that the use of fractional derivatives in epidemic models is currently widely explored, because fractional derivatives are trusted as a generalization of integer order derivatives, so modeling using fractional differential equations is a powerful method for studying the overall spread of the disease see [10, 11, 12, 13].

All inflows and outflows have been shown in the flowchart in Figure 2, and the five groups can be converted into the following system of fractional-order non-linear differential equations

$$\begin{aligned}
 \mathcal{D}^{(\sigma)}S &= \Lambda - \alpha SI - d_1S + \tau R \\
 \mathcal{D}^{(\sigma)}E &= \alpha SI - (r + \beta_1 + \sigma_3 + d_1)E \\
 \mathcal{D}^{(\sigma)}I &= rE - (\beta_2 + \sigma_2 + d_1 + d_2)I \\
 \mathcal{D}^{(\sigma)}Q &= \beta_1E + \beta_2I - (\sigma_1 + d_1 + d_2)Q \\
 \mathcal{D}^{(\sigma)}R &= \sigma_3E + \sigma_2I + \sigma_1Q - (d_1 + \tau)R
 \end{aligned}
 \tag{3}$$

with the initial conditions

$$S(0) = S_0, E(0) = E_0, I(0) = I_0, Q(0) = Q_0, R(0) = R_0,
 \tag{4}$$

where $\mathcal{D}^{(\sigma)}$ is the Caputo fractional derivative operator of order σ with $0 < \sigma < 1$, and the total population size is $N(t)$, which is defined as

$$N = S + E + I + Q + R.
 \tag{5}$$

The system (3) is called as fractional order of *SEIQR* model.

In this paper, we study the stability of the endemic and disease-free equilibriums of the model (3). In addition, we also study the effect of the addition of the quarantine compartment on the basic reproduction number and the number of infected individuals. As far as the authors know, there is still no solution to this problem. As a result, the findings of this study represent both a novel and a fresh advancement in the field of fractional-order epidemic dynamics.

The paper is organized as follows: Section 2 presents some mathematical concepts needed to analyze the stability of fractional order dynamical systems. The main result of this article is presented in the section 3. Section 4 concludes the paper.

2. PRELIMINARIES

This section contains the mathematical results needed for the analysis. For the integrable vector function $\mathbf{f} : [0, \infty) \rightarrow \mathbb{R}^n$ and $\sigma \in (i-1, i)$, $i \in \mathbb{N}$, the Caputo fractional derivative of order σ of the function \mathbf{f} is defined by

$$(6) \quad \mathcal{D}^{(\sigma)}\mathbf{f}(t) = \frac{1}{\Gamma(i-\sigma)} \int_0^t \frac{\mathcal{D}^{(i)}\mathbf{f}(s)}{(t-s)^{\sigma-i+1}} ds$$

where $\Gamma(\cdot)$ is the Euler Gamma function [14], and $\mathcal{D}^{(i)}\mathbf{f}(\cdot)$ is the usual i th derivative of function $\mathbf{f}(\cdot)$.

Let us consider the fractional-order nonlinear system involving Caputo derivative

$$(7) \quad \mathcal{D}^{(\sigma)}\mathbf{f}(t) = \mathbf{h}(t, \mathbf{f}(t))$$

with suitable initial conditions $\mathbf{f}(0) = \mathbf{f}_0$, where $\mathbf{f}(t) \in \mathbb{R}^n$ is the state vector of the system (7), $\mathbf{h} : [0, \infty) \times \mathbb{R}^n \rightarrow \mathbb{R}^n$. Specifically, the system (7) can be written as

$$(8) \quad \mathcal{D}^{(\sigma)}\mathbf{f}(t) = \mathcal{A}\mathbf{f}(t),$$

where $\mathcal{A} \in \mathbb{R}^{n \times n}$ if \mathbf{f} is linear. The point \mathbf{f}^* is said the equilibrium point of the system (7) if $\mathbf{h}(t, \mathbf{f}^*) = \mathbf{0}$.

Theorem 2.1. [15] *If $|\arg(\lambda_j)| > \frac{\sigma\pi}{2}$ for each eigenvalues λ_j , $j = 1, 2, \dots, n$ of the matrix \mathcal{A} , then the fractional-order linear system (8) with $\sigma \in (0, 1)$ is asymptotically stable*

Theorem 2.2. [15] *Let \mathbf{f}^* is an equilibrium of the the fractional-order system (7) with $\sigma \in (0, 1)$. The equilibrium point \mathbf{f}^* is asymptotically stable if*

$$(9) \quad |\arg(\lambda)| > \frac{\sigma\pi}{2},$$

for all roots λ of the equation

$$(10) \quad |\mathcal{J}_{\mathbf{f}^*} - \lambda I| = 0$$

where $\mathcal{J}_{\mathbf{f}^*}$ is the Jacobian matrix of system (7) at the equilibrium \mathbf{f}^* and I is the identity matrix.

3. MATHEMATICAL ANALYSIS OF THE SYSTEM

3.1. Boundedness of Solutions.

Theorem 3.1. *The solutions of the system (3) with initial condition (4) is uniformly bounded for all $t \geq 0$ in the following region*

$$(11) \quad \Omega = \{(S, E, I, Q, R) \in \mathbb{R}^5 : 0 < N \leq \frac{\Lambda}{d_1}\}.$$

Proof. Using (5) and (3) we have

$$(12) \quad \begin{aligned} \mathcal{D}^{(\sigma)}N &= \mathcal{D}^{(\sigma)}S + \mathcal{D}^{(\sigma)}E + \mathcal{D}^{(\sigma)}I + \mathcal{D}^{(\sigma)}Q + \mathcal{D}^{(\sigma)}R \\ &= \Lambda - d_1N - d_2(I + Q). \end{aligned}$$

Since $d_2(I + Q) \geq 0$, we have

$$(13) \quad \mathcal{D}^{(\sigma)}N + d_1N \leq \Lambda.$$

Accordance to Lemma 3 in [16], the solution of (13) is given by

$$(14) \quad N(t) \leq \left(N(0) - \frac{\Lambda}{d_1}\right) \mathbb{E}_{\sigma}(-d_1 t^{\sigma}) + \frac{\Lambda}{d_1},$$

where $\mathbb{E}_{\sigma}(-d_1 t^{\sigma}) = \sum_{k=0}^{\infty} \frac{(-d_1 t^{\sigma})^k}{\Gamma(\sigma k + 1)}$ is a Mittag-Leffler function. Therefore,

$$\limsup_{t \rightarrow \infty} N(t) \leq \frac{\Lambda}{d_1},$$

that shows that the system (3) is uniformly bounded. \square

3.2. Existence of Equilibria and Basic Reproduction Number. There are two equilibria for the model (3), namely the TB free-equilibrium (denoted by \mathcal{E}_0), and the TB endemic equilibrium (denoted by \mathcal{E}_e), both found by setting

$$(15) \quad \mathcal{D}^{(\sigma)}S = \mathcal{D}^{(\sigma)}E = \mathcal{D}^{(\sigma)}I = \mathcal{D}^{(\sigma)}Q = \mathcal{D}^{(\sigma)}R = 0,$$

The TB free-equilibrium is $\mathcal{E}_0 = \left(\frac{\Lambda}{\delta_1}, 0, 0, 0, 0\right)$ found by setting $I = 0$.

The basic reproduction number is calculated using this TB free-equilibrium. As is commonly known, the basic reproduction number, denoted as \mathfrak{R}_0 , quantifies the likelihood that a disease would spread throughout a population. . The basic reproduction number is the total number of

secondary infections that a single primary infection can cause in a fully susceptible population. The basic reproduction number can be calculated using the Next-Generation Matrix technique [17]. The matrix \mathcal{F} dan \mathcal{V} for our model are as follows:

$$\mathcal{F} = \begin{pmatrix} \alpha SI \\ 0 \\ 0 \end{pmatrix}, \mathcal{V} = \begin{pmatrix} (r + \beta_1 + \sigma_3 + d_1)E \\ -rE + (\beta_1 + \sigma_1 + d_1 + d_2)I \\ -\beta_1 E - \beta_2 I + (\sigma_1 + d_1 + d_2)Q \end{pmatrix},$$

The aforementioned matrices Jacobian, evaluated at the TB-free equilibrium point, is provided by

$$F = \begin{bmatrix} 0 & \frac{\alpha\Lambda}{d_1} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} \varepsilon_1 & 0 & 0 \\ -r & \varepsilon_2 & 0 \\ -\beta_1 & -\beta_2 & \varepsilon_3 \end{bmatrix},$$

where $\varepsilon_1 = r + \beta_1 + \sigma_3 + d_1$, $\varepsilon_2 = \beta_2 + \sigma_2 + d_1 + d_2$, $\varepsilon_3 = \sigma_1 + d_1 + d_2$. The spectral radius of the matrix FV^{-1} gives the basic reproduction number \mathfrak{R}_0 and it is given by

$$(16) \quad \mathfrak{R}_0 = \frac{\alpha\Lambda r}{d_1 \varepsilon_1 \varepsilon_2}.$$

Next, by setting $I_e > 0$, one gets the TB endemic equilibrium $\mathcal{E}_e = (S_e, E_e, I_e, Q_e, R_e)$, for which

$$S_e = \frac{\Lambda}{d_1 R_0}, E_e = \frac{d_1 \varepsilon_2 \eta (R_0 - 1)}{\alpha r (\eta - \rho)}, I_e = \frac{d_1 \eta (R_0 - 1)}{\alpha (\eta - \rho)},$$

$$Q_e = \frac{d_1 \varepsilon_1 \varepsilon_2 \varepsilon_4 (R_0 - 1) (\beta_1 \varepsilon_2 + r \beta_2)}{\alpha r (\eta - \rho)}, R_e = \frac{d_1 \varepsilon_1 \varepsilon_2 \rho (R_0 - 1)}{\alpha r \tau (\eta - \rho)},$$

where

$$(17) \quad \varepsilon_4 = d_1 + \tau, \eta = \varepsilon_1 \varepsilon_2 \varepsilon_3 \varepsilon_4, \rho = \tau \sigma_3 \varepsilon_2 \varepsilon_3 + r \tau \sigma_2 \varepsilon_3 + \tau \sigma_1 \beta_1 \varepsilon_2 + r \tau \sigma_1 \beta_2.$$

3.3. Stability Analysis. To conduct the stability analysis, we first obtain the system's Jacobian (3), as follows:

$$\mathcal{J} = \begin{bmatrix} -\alpha I - d_1 & 0 & -\alpha S & 0 & \tau \\ \alpha I & -(r + \beta_1 + \sigma_3 + d_1) & \alpha S & 0 & 0 \\ 0 & r & -(\beta_2 + \sigma_2 + d_1 + d_2) & 0 & 0 \\ 0 & \beta_1 & \beta_2 & -(\sigma_1 + d_1 + d_2) & 0 \\ 0 & \sigma_3 & \sigma_2 & \sigma_1 & -(d_1 + \tau) \end{bmatrix}$$

The Jacobian at around the TB free-equilibrium is given by the following matrix:

$$(18) \quad \mathcal{J}_{\mathcal{E}_0} = \begin{bmatrix} -d_1 & 0 & \frac{-\alpha\Lambda}{d_1} & 0 & \tau \\ 0 & -\varepsilon_1 & \frac{\alpha\Lambda}{d_1} & 0 & 0 \\ 0 & r & -\varepsilon_2 & 0 & 0 \\ 0 & \beta_1 & \beta_2 & -\varepsilon_3 & 0 \\ 0 & \sigma_3 & \sigma_2 & \sigma_1 & -\varepsilon_4 \end{bmatrix},$$

Based on the Jacobian (18) one gets the following characteristic polynomial:

$$(19) \quad (-d_1 - \lambda)(-\varepsilon_3 - \lambda)(-\varepsilon_4 - \lambda)p(\lambda) = 0,$$

where $p(\lambda) = \lambda^2 + (\varepsilon_1 + \varepsilon_2)\lambda + \varepsilon_1\varepsilon_2(1 - \mathfrak{R}_0)$. The Jacobian matrix $\mathcal{J}_{\mathcal{E}_0}$ possesses the five eigenvalues that given by $\lambda_1 = -d_1, \lambda_2 = -\varepsilon_3, \lambda_3 = -\varepsilon_4$ and λ_4 and λ_5 are the roots of $p(\lambda)$. One can easily get that the roots of $p(\lambda)$ are

$$(20) \quad \lambda_{4,5} = \frac{1}{2} \left(-(\varepsilon_1 + \varepsilon_2) \pm \sqrt{(\varepsilon_1 + \varepsilon_2)^2 + 4\varepsilon_1\varepsilon_2(\mathfrak{R}_0 - 1)} \right).$$

It is obvious that eigenvalues λ_i , for $i = 1, 2, 3$ are negative, thus they satisfy $|\arg(\lambda_i)| > \frac{\sigma\pi}{2}$, whereas $|\arg(\lambda_{4,5})| > \frac{\sigma\pi}{2}$ if $\mathfrak{R}_0 < 1$, and it implies $|\arg(\lambda_{3,4})| < \frac{\sigma\pi}{2}$ when $\mathfrak{R}_0 > 1$. Hence, based on the Theorem 2.2, \mathcal{E}_0 is asymptotically stable if $\mathfrak{R}_0 < 1$ and becomes unstable if $\mathfrak{R}_0 > 1$.

Furthermore, the Jacobian at around the TB endemic equilibrium \mathcal{E}_e is given by

$$(21) \quad \mathcal{J}_{\mathcal{E}_e} = \begin{bmatrix} -\alpha I^* - d_1 & 0 & -\alpha S^* & 0 & \tau \\ \alpha I^* & -\varepsilon_1 & \alpha S^* & 0 & 0 \\ 0 & r & -\varepsilon_2 & 0 & 0 \\ 0 & \beta_1 & \beta_2 & -\varepsilon_3 & 0 \\ 0 & \sigma_3 & \sigma_2 & \sigma_1 & -\varepsilon_4 \end{bmatrix},$$

Based on the Jacobian (21) one gets the following characteristic polynomial:

$$(22) \quad \lambda^5 + a_1\lambda^4 + a_2\lambda^3 + a_3\lambda^2 + a_4\lambda + a_5 = 0,$$

where

$$a_1 = \alpha I^* + d_1 + \varepsilon_1 + \varepsilon_2 + \varepsilon_3 + \varepsilon_4,$$

$$a_2 = \varepsilon_1\varepsilon_2 - \alpha S^*r + (\alpha I^* + d_1 + \varepsilon_3 + \varepsilon_4)(\varepsilon_1 + \varepsilon_2) + (\alpha I^* + d_1)(\varepsilon_3 + \varepsilon_4) + \varepsilon_3\varepsilon_4,$$

$$a_3 = (\alpha I^* + d_1 + \varepsilon_3 + \varepsilon_4)(\varepsilon_1\varepsilon_2 - \alpha S^*r) + (\varepsilon_1 + \varepsilon_2)((\alpha I^* + d_1)(\varepsilon_3 + \varepsilon_4) + \varepsilon_3\varepsilon_4) + (\alpha I^* + d_1)\varepsilon_3\varepsilon_4 + \alpha I^*(\alpha S^*r - \tau\sigma_3),$$

$$a_4 = (\varepsilon_1\varepsilon_2 - \alpha S^*r)((\alpha I^* + d_1)(\varepsilon_3 + \varepsilon_4) + \varepsilon_3\varepsilon_4) + (\varepsilon_1 + \varepsilon_2)\varepsilon_3\varepsilon_4(\alpha I^* + d_1) + \alpha I^*(\alpha S^*r(\varepsilon_3 + \varepsilon_4) - \tau(r\sigma_2 + \beta_1\sigma_1 + \sigma_3\varepsilon_2 + \sigma_3\varepsilon_3)),$$

$$a_5 = (\alpha I^* + d_1)\varepsilon_3\varepsilon_4(\varepsilon_1\varepsilon_2 - \alpha S^*r) + \alpha I^*(\alpha S^*r\varepsilon_3\varepsilon_4 - \tau(r\beta_2\sigma_1 + r\sigma_2\varepsilon_3 + \beta_1\sigma_1\varepsilon_2 + \sigma_3\varepsilon_2\varepsilon_3)).$$

Using the *Routh-Hurwitz's* criteria, the the real part of eigenvalues λ_i , $i = 1, 2, 3, 4, 5$ of the matrix $\mathcal{J}_{\mathcal{E}_e}$ are negative if

- (i). $a_1 > 0$,
- (ii). $a_1a_2 - a_3 > 0$,
- (iii). $a_1a_2a_3 - a_1^2a_4 - a_3^2 + a_5a_1 > 0$,
- (iv). $a_1a_2a_3a_4 - a_5a_1a_2^2 - a_1^2a_4^2 + 2a_5a_1a_4 - a_3^2a_4 + a_5a_2a_3 - a_5^2 > 0$,
- (v). $a_1a_2a_3a_4a_5 - a_5^2a_1a_2^2 - a_5a_1^2a_4^2 + 2a_5^2a_1a_4 - a_5a_3^2a_4 + a_5^2a_2a_3 - a_5^3 > 0$.

and this is satisfied if $\mathfrak{R}_0 > 1$. This implies $|\arg(\lambda_i)| > \frac{\sigma\pi}{2}$ for $i = 1, 2, 3, 4$ when $\mathfrak{R}_0 > 1$. Hence, based on the Theorem 2.2, \mathcal{E}_e is asymptotically stable if $\mathfrak{R}_0 > 1$ and becomes unstable if $\mathfrak{R}_0 < 1$.

3.4. Numerical Simulation. In order to show the validity of the results, in the following we present a numerical simulation.

For the model (3), let $\Lambda = 123381$, $\tau = 0.1111$, $\alpha = 0.00000007$, $\beta_1 = 0.25$, $\beta_2 = 0.18$, $\sigma_1 = 0.1$, $\sigma_2 = 0.0714$, $\sigma_3 = 0.2$, $r = 0.2$, $d_1 = 0.0035$, $d_2 = 0.0825$. The initial conditions are $S(0) =$

40214389; $E(0) = 503911$; $I(0) = 135388$; $Q(0) = 59638$; $R(0) = 81289$. Based on these parameter values, we find that the TB-endemic equilibrium point $\mathcal{E}_e = (1.5749 \times 10^7, 2.9338 \times 10^5, 1.7391 \times 10^5, 5.6263 \times 10^5, 1.1113 \times 10^6)$ and $\mathfrak{R}_0 = 2.2383$. In other case, if we fix $\beta_1 = \beta_2 = \sigma_1 = 0$ (without flow toward the quarantine compartment) such that (3) becomes the *SEIR* model, we have the TB-endemic equilibrium point $\mathcal{E}_e = (4.5365 \times 10^6, 8.8368 \times 10^5, 1.1228 \times 10^6, 0, 2.2418 \times 10^6)$ and $\mathfrak{R}_0 = 7.7707$.

This fact shows that the absence of a quarantine compartment increases the number of basic reproduction. One can see that the TB-endemic equilibrium \mathcal{E}_e is asymptotic stable in both cases due to $\mathfrak{R}_0 > 1$. Moreover, the convergence of the TB-endemic equilibrium point becomes faster as the fractional order increases. Graphs the susceptible subpopulation, exposed subpopulation, infected subpopulation, quarantine subpopulation and recovery subpopulation of both cases for several fractional order are given in Figure 3 and Figure 4. In Figure 4, it can be seen that the number of sub-populations in the quarantine compartment is gradually zero, this is due the initial sub-population $Q(0) \neq 0$.

4. CONCLUSION

We have established a fractional order *SEIQR* mathematical model for Tuberculosis (TB) spread in a human population. It was shown that the stability of the equilibrium points depends on the basic reproduction number, and the addition of the quarantine sub-population compartment decreases the number of basic reproduction. It has shown that the TB free-equilibrium is asymptotically stable if $\mathfrak{R}_0 < 1$; otherwise, it is unstable. The TB endemic-equilibrium is asymptotically stable if $\mathfrak{R}_0 > 1$, otherwise it is unstable.

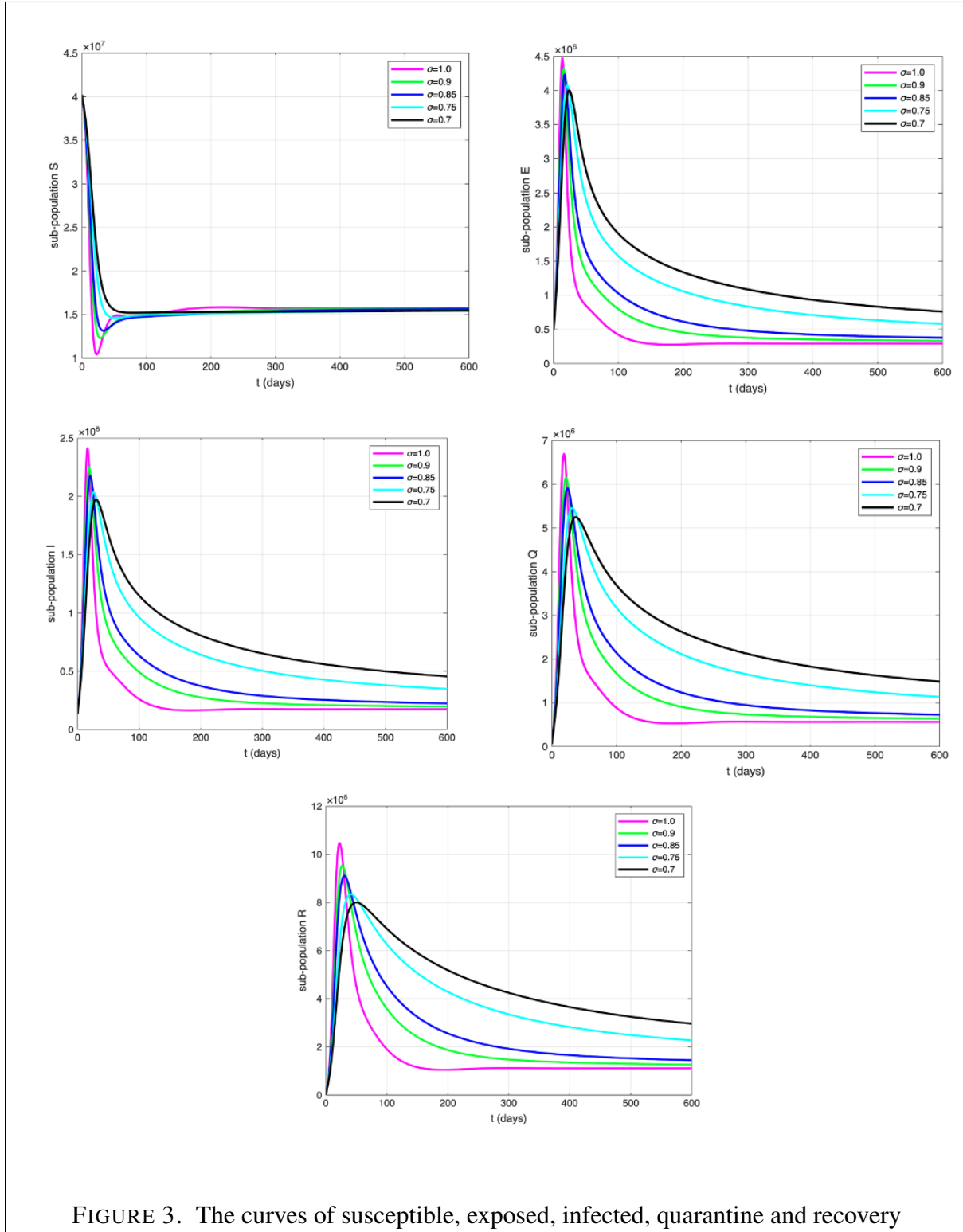


FIGURE 3. The curves of susceptible, exposed, infected, quarantine and recovery

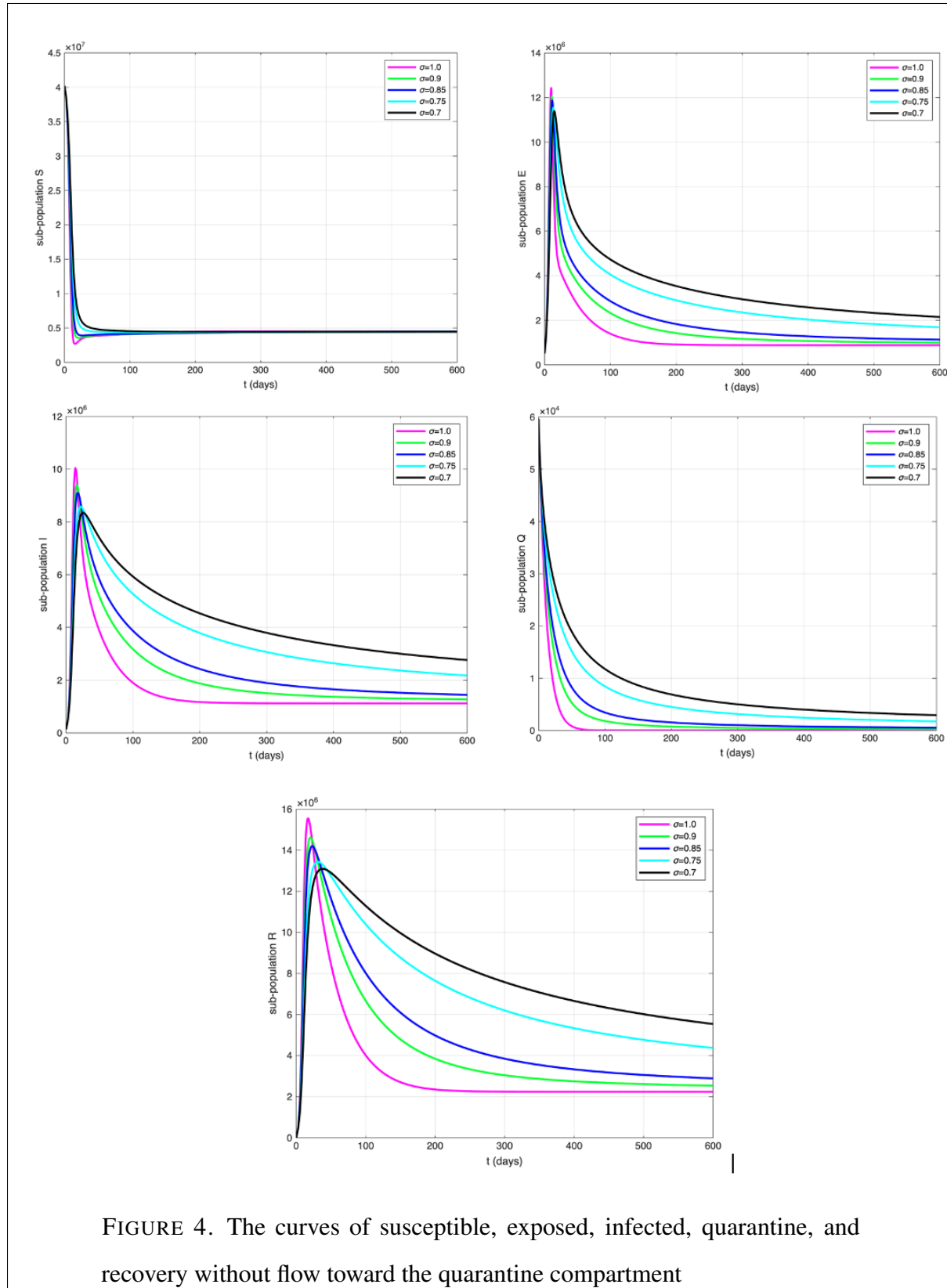


FIGURE 4. The curves of susceptible, exposed, infected, quarantine, and recovery without flow toward the quarantine compartment

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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