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The effect of vaccination and treatment of measles disease described by a fractional order model

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Abstract. In this work, we consider the fractional-order Susceptible-Infected-Recovered (SIR) epidemic model with vital dynamics, which is used to describe measles disease. We show that the model established in this paper possesses non-negative solutions as desired in any population dynamics. The stability of equilibrium points is studied. We carried out numerical solutions to verify the theoretical analysis by applying Fractional Euler method (FEM).

Keywords: fractional differential equations, mathematical model, stability, fractional Euler method

1 Introduction

Measles occurs worldwide, control effort have essentially altered the global distribution[1]. Measles incidence has decreased obviously in regions where vaccination has been instituted; measles in the developing world has been attributed to low vaccination rates[2]. Worldwide, measles vaccination has been very effective, reducing measles death by 75% from an estimated 544 200 death in 2000 to 145 700 in 2013[3]. Measles outbreaks can result in epidemics that cause many death, especially among young, malnourished children. There is no specific antiviral treatment that kill the measles virus but focusing on supportive care can relief severe complications from measles, this includes; getting plenty of water, and medication to control fever or pain.

Mathematical modelling in epidemiology provides new aspect of understanding the spread of measles disease. Some examples on the use of mathematical model for analysis of treatment and control of measles disease can be found in [4–11], but most of these dynamics has been limited to ordinary differential equations. In recent years, it has turned out that many phenomena in different fields can be described very successfully by the model using fractional order differential equations (see e.g. [12–14]). Now, we consider the following model

$$\begin{cases} S'(t) = b - \beta S(t)I(t) - (d+\mu_1)S(t), \\ I'(t) = \beta S(t)I(t) - (\mu_2 + d + \sigma)I(t), \\ R'(t) = \mu_1 S(t) + \mu_2 I(t) - dR(t), \end{cases} \tag{1}$$

where $S(t)$, $I(t)$ and $R(t)$ represents the numbers of susceptible, infected and recovered individuals at time t, respectively. Here, b is the birth (recruitment) rate, β is the disease transmission rate between infected and susceptible, d is the natural death rate, μ_1 is the proportion of the susceptible that is vaccinated per unit time, μ_2 is the proportion of infections that is treated per unit time, σ is the disease-induced death rate.

The total population $N(t)$ can be obtained from $N(t) = S(t) + I(t) + R(t)$ or, by adding the right-side of (1), we have

$$N'(t) = b - d\,N(t) - \sigma I(t).$$

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This means that the population size is not constant (i.e. variable population size). Since $R(t)$ can always be obtained by the equation $R(t) = N(t) - S(t) - I(t)$. So, we have the following system

$$\begin{cases} S'(t) = b - \beta S(t)I(t) - (d + \mu_1)S(t), \\ I'(t) = \beta S(t)I(t) - (\mu_2 + d + \sigma)I(t), \\ N'(t) = b - dN(t) - \sigma I(t), \end{cases} \tag{2}$$

under initial conditions

$$S(t_0) = S_0, \quad I(t_0) = I_0, \quad N(t_0) = N_0. \tag{3}$$

Now we introduce fractional-order for the system above, where $D^\alpha S$, $D^\alpha I$ and $D^\alpha N$ are the derivatives of $S(t)$, $I(t)$, and $N(t)$ respectively, of arbitrary order α (where $0 < \alpha \leq 1$) in the sense of Caputo (see e.g. [15]), then the new system is described by the following set of fractional order differential equations

$$\begin{cases} D^\alpha S(t) = b - \beta S(t)I(t) - (d + \mu_1)S(t), \\ D^\alpha I(t) = \beta S(t)I(t) - (\mu_2 + d + \sigma)I(t), \\ D^\alpha N(t) = b - dN(t) - \sigma I(t), \end{cases} \tag{4}$$

subject to the same initial conditions given in (3). The main reason that leads to this extension (typically with α chosen close to 1) is to reduce the error that may arise from neglected parameters or simplifications in the model (2). When measles outbreak occur, the predicted number of individuals who are infected and recovered due to the vaccination by the model (2) might be significantly different (less or more) than the realistic data. Hence the fractional model (4) possess memory. So, we will use the fractional order (where memory effects are important) model (4) in order to analyze and evaluate the disease. In general, fractional differential equations (FDEs) gives a more realistic way to model disease dynamics. Also, FDEs are generalization of integer order differential equations and one of the basic reasons of using FDEs is that[16, 17] "Fractional order differential equations are, at least, as stable as their integer order counterpart". In fact, this work represents the first available numerical solution for a SIR model of fractional order for describing measles disease.

In this paper we intend to solve the model (4) by discrete method for FDEs, which offer accurate solution during a long time interval. This may be important in order to show the effect of vaccination μ_1 and treatment μ_2 of the fractional order model (4).

The rest of the paper is organized as follow. In Section 2, a brief review of the fractional calculus is presented. In Section 3, we show that the model (4) possesses a unique solution which is non-negative. Section 4 is devoted to study the equilibrium points and the stability analysis of differential equations of fractional order. Numerical simulations are represented graphically and discussed in Section 5.

2 Preliminaries

In this section, we will present some necessary definitions and notations related to fractional calculus (see e.g. [15]). The most commonly used definitions are Riemann-Liouville and Caputo.

Definition 1. *The Riemann-Liouville fractional integration of order α is defined as:*

$$\begin{aligned} (J^\alpha_{t_0} f)(t) &= \frac{1}{\Gamma(\alpha)} \int_{t_0}^{t} (t-s)^{\alpha-1} f(s) ds, \ \alpha > 0, \ t > t_0, \\ (J^0_{t_0} f)(t) &= f(t). \end{aligned}$$

Definition 2. *The Riemann-Liouville derivative of order $0 < \alpha < 1$ is defined as (see e.g. [18]:*

$$(D^\alpha_{t_0} f)(t) = \frac{1}{\Gamma(1-\alpha)} \frac{d}{dt} \int_{t_0}^{t} (t-s)^{-\alpha} f(s) ds, \ t > t_0.$$

The Riemann-Liouville derivative has certain disadvantages such that the fractional derivative of a constant is not zero. Therefore, we will make use of Caputo's definition owing to its convenience for initial conditions of the FDE. It also help us to find a connection between what is likely and what is realistic.

Definition 3. *The Caputo fractional derivative of order* $0 < \alpha < 1$ *is defined as:*

$$(D_{t_0}^{\alpha} f)(t) = \frac{1}{\Gamma(1-\alpha)} \int_{t_0}^{t} (t-s)^{-\alpha} f'(s) ds, \ t > t_0,$$

where f is a given function, and $\Gamma(\cdot)$ denotes the gamma function. It is known that $(D_{t_0}^{\alpha} f)(t) \to f'(t)$ as $\alpha \to 1$. Therefore, fractional derivative is a nonlocal operator (as it is defined on an interval), i.e. calculating time-fractional derivative of a function $f(t)$ at some time $t = t_1$ requires all the previous history.

Now, we recall the definitions of Laplace transform of Caputo's derivative and Mittag-Leffler function in two arguments.

Definition 4.

$$\begin{aligned} \mathcal{L}\{D^{\alpha} f(t), s\} &= s^{\alpha} F(s) - \sum_{i=0}^{n-1} s^{\alpha-i-1} f^{(i)}(0), \ \ (n-1 < \alpha \leq n); \ n \in \mathbb{N}. \\ E_{a,b}(x) &= \sum_{n=0}^{\infty} \frac{x^n}{\Gamma(an+b)}, \ a > 0, \ b > 0. \end{aligned}$$

2.1 Non-negative solutions

Let $\mathbb{R}^3_+ = \{X \in \mathbb{R}^3 | X \geq 0\}$ and $X(t) = (S(t), I(t), N(t))^T$, we now prove the main theorem.

Theorem 1. *There is a unique solution* $X(t) = (S(t), I(t), N(t))^T$ *for model (4) at* $t \geq 0$ *(where,* $t_0 = 0$*) and the solution will remain in* $\mathbb{R}^3_+$.

Proof. From Theorem 3.1 and Remark 3.2 of [19], we know that the solution on $(0, \infty)$ is existent and unique. Now, we will show that the feasible region $\mathbb{R}^3_+$ is positively invariant (non-negative solutions). Rearranging the last equation for the system (4) and we assume that $g(t) = b - \sigma I$ is a constant function of time. Then we get the fractional order differential equation representing the total population as follows:

$$D^{\alpha} N(t) + d\, N(t) = g(t). \tag{5}$$

Solving equation (5) using Laplace transform (from Definition 4) method[15] and taking the initial condition to be zero (to simplify), we have the following solution

$$N(t) = \int_0^t (t-\tau)^{\alpha-1} E_{\alpha,\alpha}(-d\,(t-\tau)^{\alpha}) g(\tau) d\tau \ \geq 0,$$

where $0 < \alpha < 1$, $d > 0$ and $E_{a,b}(x)$ is the two-parameter Mittag-Leffler function (see Definition 4). Since Mittag-Leffler function is an entire function[15] thus $E_{\alpha,\alpha}(-d(t-\tau)^{\alpha})$ is bounded for all $t > 0$. Therefore, as $n \to \infty$ and $t \to \infty$, we have $N \leq \frac{b}{d}$. For $S(t)$, $I(t)$ by the same way we have $S(t) \geq 0$ and $I(t) = 0$, hence proved that the solution $X(t)$ is positive invariant.

3 Equilibrium points and their asymptotic stability

To determine the stability analysis of the model (4), we first evaluate the equilibrium points or steady states of the system of the FDEs (4). The equilibrium points involved determine the disease-free (where $I = 0$) and endemic (where $I \neq 0$). To evaluate the equilibrium points, let

$$\begin{cases} D^{\alpha} S = 0, \\ D^{\alpha} I = 0, \\ D^{\alpha} N = 0, \end{cases} \tag{6}$$

then, the system (4) has two equilibrium points

1. *At disease-free equilibrium:*

We now consider the equations below and solve for the values S and N, since at this point there is no infection, thus from (6)

$$b - \beta SI - (d + \mu_1)S = 0, \tag{7}$$
$$\beta SI - (\mu_2 + d + \sigma)I = 0, \tag{8}$$
$$b - dN - \sigma I = 0. \tag{9}$$

From equation (8), we have $I = 0$, then by substituting in equations (7), (9). Then disease-free equilibrium (DFE) of the system (4) is

$$\varepsilon_1 = (S_{eq}, I_{eq}, N_{eq})_{I=0} = \left(\frac{b}{d+\mu_1},\ 0,\ \frac{b}{d}\right).$$

Using the next-generation operator approach[20, 21], we derive the expression of the basic reproduction number $\mathcal{R}_0$ (see e.g. [22]), allied to the DFE (i.e. ε_1). Following, [20, 21], the next generation matrix is given by (FV^{-1}). Then, we can compute the basic reproduction number as follow:

$$\mathcal{R}_0 = \rho(FV^{-1}),$$

where ρ denotes the eigenvalue of largest magnitude or spectral radius. First, we re-order the system of equation (4) to get

$$\begin{aligned} f_1(I, S, N) &= \beta SI - (\mu_2 + d + \sigma)I, \\ f_2(I, S, N) &= b - \beta SI - (d + \mu_1)S, \\ f_3(I, S, N) &= b - dN - \sigma I. \end{aligned}$$

Linearization of the above system gives the generation matrix (G) evaluated at the DFE,

$$G = \begin{bmatrix} f_1 I & f_1 S & f_1 N \\ f_2 I & f_2 S & f_2 N \\ f_3 I & f_3 S & f_3 N \end{bmatrix}.$$

Since f_1 and f_2 form a subsystem describing the generation and transition of infectious, the Jacobian matrix associated with the linearized subsystem at DFE is given by,

$$J_{DFE}(I, S) = \begin{bmatrix} \beta S_{eq} - (\mu_2 + d + \sigma) & 0 \\ -\beta S_{eq} & -(d + \mu_1) \end{bmatrix}.$$

J_{DFE} is decomposed as $F - V$, where the non-negative matrix F, representing the matrix of new infection and the non-singular matrix V, representing transmission term of different infected compartments of the model (4), i.e.

$$F = \begin{bmatrix} \beta S_{eq} & 0 \\ 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \mu_2 + d + \sigma & 0 \\ \beta S_{eq} & (d + \mu_1) \end{bmatrix}.$$

Thus, the next generation matrix becomes

$$FV^{-1} = \begin{bmatrix} \frac{b\beta}{(d+\mu_1)(\mu_2+d+\sigma)} & 0 \\ 0 & 0 \end{bmatrix},$$

where we have $S_{eq} = \frac{b}{d+\mu_1}$ at DFE. Since $\mathcal{R}_0 = \rho(FV^{-1})$, then

$$\mathcal{R}_0 = \frac{b\beta}{(d+\mu_1)(\mu_2+d+\sigma)}. \tag{10}$$

2. *At endemic equilibrium:*

We now consider the case where there is infection, thus from equation (8) $S = \frac{\mu_2+d+\sigma}{\beta}$ by substituting in equations (7) and (9), then we have

$$\varepsilon_2 = (S_{eq}, I_{eq}, N_{eq})_{I\neq 0} = (S^*, I^*, N^*)$$

where

$$\begin{aligned} S^* &= \frac{\mu_2+d+\sigma}{\beta}, \\ I^* &= (\mathcal{R}_0 - 1)\frac{\mu_1+d}{\beta}, \\ N^* &= \frac{b\beta(\mu_2+d)+\sigma(\mu_1+d)(\mu_2+d+\sigma)}{d\beta(\mu_2+d+\sigma)}. \end{aligned}$$

We can note that the equilibrium points are the same for both integer and fractional system. But the stability region of the fractional-order system with order α, which is illustrated in Figure 1 (where σ, ω refer to the real and imaginary parts of the eigenvalues, respectively, and $j = \sqrt{-1}$), is greater than the stability region of the integer order case (see e.g.[23]). Therefore, we will now drive analytically the stability of different equilibria

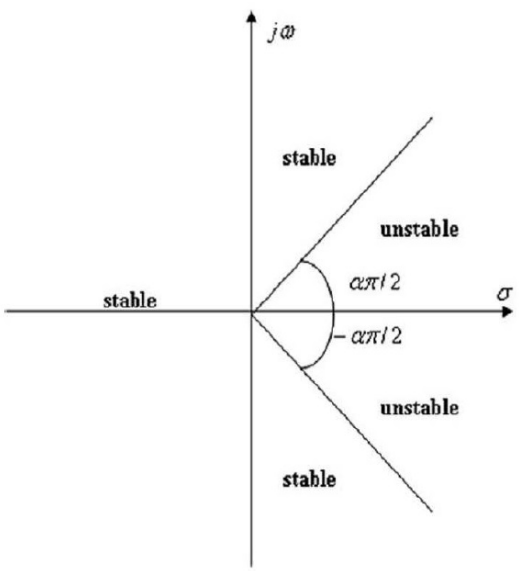

Fig. 1: Stability region of the fractional-order system

of the model (4). For ε_1 and the expression (10) of $\mathcal{R}_0$, we have the following theorem:

Theorem 2. *The disease free equilibria ε_1 of the system (4) is locally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. Determining the Jacobian matrix of the system (4) at ε_1 we have:

$$J_{\varepsilon_1} = \begin{bmatrix} -d-\mu_1 & \frac{-b\beta}{d+\mu_1} & 0 \\ 0 & \frac{b\beta}{d+\mu_1} - \mu_2 - d - \sigma & 0 \\ 0 & -\sigma & -d \end{bmatrix}.$$

The eigenvalues of J_{ε_1} are

$$\lambda_1 = -(d+\mu_1) < 0,\ \lambda_3 = -d < 0,\ \lambda_2 = \frac{b\beta}{d+\mu_1} - (\mu_2 + d + \sigma).$$

Now, we should give the following remark to continue with our proof.

Remark 1. Disease free equilibrium ε_1 of the system (4) is locally asymptotically stable if $|\arg(\lambda_i)| > \frac{\alpha\pi}{2},\ \forall\, i = 1, 2, 3$ (see e.g. [24, 25]).

If $\mathcal{R}_0 = \frac{b\beta}{(d+\mu_1)(\mu_2+d+\sigma)} < 1$, then $\frac{b\beta}{d+\mu_1} < (\mu_2 + d + \sigma) \Rightarrow \lambda_2 < 0$ and therefore, $|\arg(\lambda_i)| > \frac{\alpha\pi}{2},\ \forall\, i = 1, 2, 3$. Thus, disease free equilibrium ε_1 of the system (4) is locally asymptotically stable if $\mathcal{R}_0 < 1$.

For ε_2, we have the following theorem:

Theorem 3. *The endemic equilibrium point ε_2 is locally asymptotically stable if $\mathcal{R}_0 > 1$.*

Proof. The Jacobian matrix evaluated at the endemic equilibrium gives

$$J_{\varepsilon_2} = \begin{bmatrix} -\mathcal{R}_0(\mu_1 + d) & -(d + \mu_2 + \sigma) & 0 \\ (\mathcal{R}_0 - 1)(\mu_1 + d) & 0 & 0 \\ 0 & -\sigma & -d \end{bmatrix}$$

and its eigenvalues are

$$\lambda_1 = -d < 0,\ \lambda_{2,3} = \frac{-\mathcal{R}_0(\mu_1 + d) \pm \sqrt{\mathcal{R}_0^2(\mu_1 + d)^2 - 4(\mathcal{R}_0 - 1)(\mu_1 + d)(d + \mu_2 + \sigma)}}{2}.$$

This shows that if $\mathcal{R}_0 > 1$, then $\lambda_2 < 0$ and $\lambda_3 < 0$, hence it becomes asymptotically stable.

4 Numerical method and results

In this section we present the method used in the paper. For instance, considering the general initial value problem

$$D^\alpha y(t) = f(t, y(t)), \quad y(t_0) = y_0, \quad 0 < \alpha \leq 1, \quad t_0 < t \leq T. \tag{11}$$

In a discrete numerical method the time interval $[t_0, T]$ is replaced by a discrete set of points $t_j = t_0 + jh$, $h = \frac{T - t_0}{N}$, $j = 0, 1, ..., N$, so that the solution is approximated by a sequence $\{y_j\}_{j=0,1,...,N}$ such that $y_j \approx y(t_j)$. The exact solution of (11) can be written in terms of a Volterra integral equation of the second kind with a weakly singular kernel,

$$y(t) = y(t_0) + \frac{1}{\Gamma(\alpha)} \int_{t_0}^{t} (t - s)^{\alpha-1} f(s, y(s)) ds. \tag{12}$$

The method is based on the approximation of the integral on the right-hand side of equation (12) by the product rectangle rule. This leads to the formula

$$y_k = y_0 + \frac{h^\alpha}{\Gamma(\alpha + 1)} \sum_{j=0}^{k-1} b_{j,k} f(t_j, y_j), \tag{13}$$

for $k = 1, 2, ..., N$ where the weights

$$b_{j,k} = (k - j)^\alpha - (k - 1 - j)^\alpha.$$

In the limit case $\alpha \to 1$ the generalized one-step Adams-Bashforth method (that is, the Fractional Euler method) reduces to the classical first-order Adams-Bashforth formula (that is, the forward Euler method). It is an explicit method since y_k doesn't appear on the right-hand side of (13). As a consequence of Corollary 2.1 in [26], the error can be estimated as follows:

Theorem 4. *The approximation computed by the Adams-Bashforth method satisfies the error bound*

$$|y(t_j) - y_j| = O(h)$$

uniformly for all j *if* $D^\alpha y \in C^1[0, T]$.

Now, we will study the effect of vaccination μ_1 and treatment μ_2 on the dynamics of measles disease described by the fractional-order model (4) using the formula (13). The following values, for parameters (see [11]), are considering

$$b = 0.03, \;\; d = 0.02, \;\; \sigma = 0.1, \;\; \beta = 0.75, \;\; S_0 = 0.95, \;\; I_0 = 0.05, \;\; N_0 = 1. \tag{14}$$

From this values of parameters, we estimate that $\mathcal{R}_0 = \frac{0.0225}{(\mu_1+0.02)(\mu_2+0.12)}$. The approximate solutions displayed in Figs.2-4 for step size $h = 0.1$ with different value of fractional order $0 < \alpha \leq 1$ and it is clear that varying the values of μ_1 and μ_2 will alter the number of susceptible and infected persons. If $\mu_1 = \mu_2 = 0$ (i.e. in the absence of vaccination and treatment), then $\mathcal{R}_0 = 9.3750 > 1$ and from the results the disease will persist, while in the beginning of time interval the number of susceptible decrease (see Fig.2(a)), the number of infected increases (see Fig.2(b)) and in Fig.2(c) we can note that $N(t)$ never goes to extinction, this is the main reason for chosen these values of parameters (14). If $\mu_1 = \mu_2 = 1$ (i.e. in the presence of vaccination and treatment), $\mathcal{R}_0 = 0.0197 < 1$, the number of susceptible dramatically decreased due to the population have been already vaccinated (see Fig.4(a)) and the infection will die out (see Fig.4(b)). About the relevance of vaccination and treatment is obvious from Fig.3. For the fractional order case, in Fig.2(b) the climax of $I(t)$ is reduced. But the disease takes a longer time to be eradicated (see Fig.4(b)). From the numerical results in Figs.2-4, it is clear that the approximate solutions continuously depends on the time-fractional derivative α.

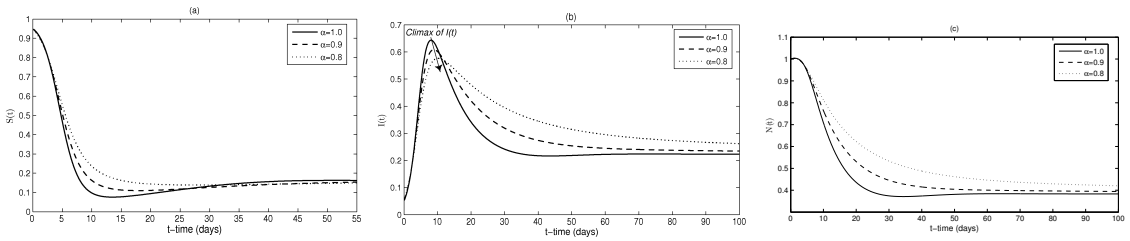

Fig. 2: (a) $S(t)$, (b) $I(t)$, (c) $N(t)$ versus t with different values of α and $\mathcal{R}_0 > 1$.

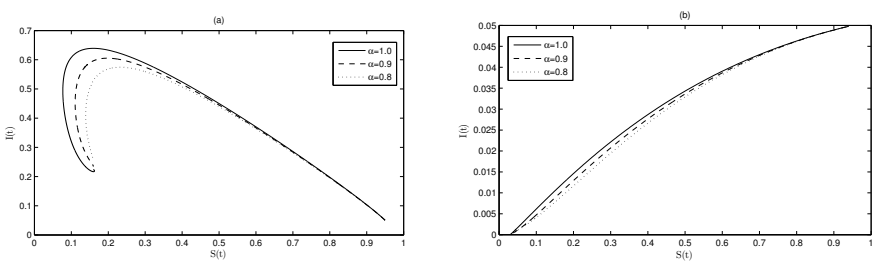

Fig. 3: $I(t)$ versus $S(t)$ with different values of α where (a) $\mathcal{R}_0 > 1$ and (b) $\mathcal{R}_0 < 1$.

5 Conclusion

In this paper we have been able to extend the ODE model (2) to take care of all the properties and also the principle of the proposed model (4) possess memory. We obtained the non-negative solutions of the fractional model by Laplace transform. The numerical results confirmed that in the absence of vaccination and treatment

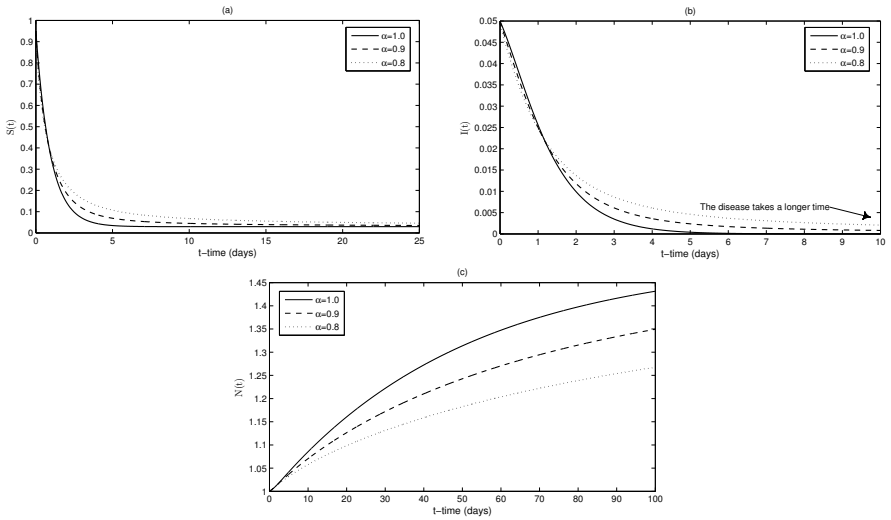

Fig. 4: (a) $S(t)$, (b) $I(t)$, (c) $N(t)$ versus t with different values of α and $\mathcal{R}_0 < 1$.

the disease persists while in the presence of vaccination and treatment the disease die out. We recommend that the public health sector can used the proposed model (4) to understand the spread and control of measles. We also need to mention that when dealing with epidemic diseases in a population, the order of the fractional system can be determined by using the collected data.

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