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Comparative Study for Multi-Strain Tuberculosis (TB) Model of Fractional Order

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Abstract: In this paper, we introduce the multi−strain TB model of fractional-order derivatives, which incorporates three strains: drug−sensitive, emerging multi−drug resistant(MDR) and extensively drug−resistant(XDR). Numerical simulations for this extended fractional order model is the main aim of this work, where the adopted model is described by a system of non-linear ordinary differential equations and the fractional derivative is defined in the sense of the Grünwald−Letnikov definition. Two numerical methods are presented for this model, the standard finite difference method (SFDM) and the nonstandard finite difference method (NSFDM). Numerical comparisons between SFDM and NSFDM are presented. It is concluded that the proposed NSFDM preserves the positivity of the solutions, and it is numerically stable in large regions than SFDM.

Keywords: Nonstandard finite difference; Epidemic model; Tuberculosis; M/XDR−TB; Fractional differential; Grünwald−Letnikov definition.

1 Introduction

Recently, fractional calculus has gained an increasing popularity due to the wide range of applications in fields including biology, engineering, chemistry, finance, physics and so on ([16],[22]−[26]). Consequently mathematical models have become important tools in analyzing the spread and control of infectious diseases. Understanding the transmission characteristics of infectious diseases in communities, regions and countries can lead to better approaches to decrease the transmission of these diseases [7]. Tuberculosis(TB) is an infectious respiratory disease caused by the bacteria Mycobacterium tuberculosis. It is considered as one of the most important infectious diseases, and important health issue all over the world, particularly in many African countries. TB is growing more resistant to treatment worldwide according to study released in August 2012 in the journal LANCET, a finding that suggest the potentially fatal disease is becoming more difficult and costly to treat [27]. We consider in this work a model developed by J. Arino and I. Soliman for TB [2]. The model incorporates three strains, drug−sensitive, MDR and XDR. Several papers considered modeling TB such as ([3], [4], [5], [17], [21], [28]), but the model we consider here includes several factors of spreading TB such as the fast infection, the exogenous reinfection and secondary infection along with the resistance factor.The reasons for considering a fractional order TB−system are:

– Fractional order differential equations are generalizations of integer order differential equations.

– We like to argue that fractional order equations are more suitable than integer order ones in modeling biological, economic and social systems (generally complex adaptive systems) where memory effects are important.

We develop NSFDM for solving fractional model for tuberculosis (TB) that incorporates three strains, i.e., drug−sensitive and MDR and XDR model. The adopted model is described by system of non-linear ordinary differential equation. Numerical comparison between NSFDM and SFDM are presented. When the secondary infection generated by an infected individual exceeds the unity, there are no analytical results proved for the model, such as the existence and stability of the endemic equilibrium (EE). In this case we use the developed NSFDM to approximate the endemic solution numerically and investigate its stability. Furthermore,

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with the help of the NSFDM , we answer the following question: Given the data provided by the World Health Organization (2012) on the current parameters corresponding to the propagation of the TB in Egypt, What would be the required rate of treatment to achieve in order to control the disease?. The proposed method showed its superiority in preserving the positivity (compared to the numerical standard method considered in this work) of the state variables of the systems under study. This is an essential requirement when simulating systems especially those arising in biology. This paper is organized as follows: In section 2, the mathematical model is presented. Preliminaries and notations on fractional differential equations and NSFD discretization are given, in section 3. Equilibrium points and their asymptotic stability are presented in section 4. In section 5, fractional−order of multi−strain TB model are presented moreover, the construction of the proposed nonstandard numerical scheme is carried out. In section 6, numerical simulations equilibria are discussed. Finally, in section 7, we presented the conclusions.

2 Mathematical Model

In this section, we introduce the multi-strain TB model which is given in [2], this model incorporates three strains: drug-sensitive, MDR, XDR. The population of interest is divided into eight compartments, see Table 1. Adopted model is described by a system of nonlinear ordinary differential equations as follows:

$$\dot{S} = b - dS - \beta_s\frac{SI_s}{N} - \beta_m\frac{SI_m}{N} - \beta_x\frac{SI_x}{N}, \quad (1)$$

$$\dot{L_s} = \lambda_s\beta_s\frac{SI_s}{N} + \sigma_s\lambda_s\beta_s\frac{RI_s}{N} - \alpha_{ss}\beta_s\frac{L_sI_s}{N} - \alpha_{sm}\beta_m\frac{L_sI_m}{N} - \alpha_{sx}\beta_x\frac{L_sI_x}{N} + \gamma_sI_s - (d+\varepsilon_s+t_{1s})L_s, \quad (2)$$

$$\dot{L_m} = \lambda_m\beta_m\frac{SI_m}{N} + \sigma_m\lambda_m\beta_m\frac{RI_m}{N} + \alpha_{sm}\beta_m\lambda_m\frac{L_sI_m}{N} - \alpha_{mm}\beta_m\frac{L_mI_m}{N} - \alpha_{mx}\beta_x\frac{L_mI_x}{N} - (d+\varepsilon_m)L_m + (1-P_1)t_{1s}L_s + (1-P_2)t_{2s}I_s + \gamma_mI_m, \quad (3)$$

$$\dot{L_x} = \lambda_x\beta_x\frac{SI_x}{N} + \sigma_x\lambda_x\beta_x\frac{RI_x}{N} + \alpha_{sx}\beta_x\lambda_x\frac{L_sI_x}{N} + \alpha_{mx}\beta_x\lambda_x\frac{L_mI_x}{N} - \alpha_{xx}\beta_x\frac{L_xI_x}{N} - (d+\varepsilon_x)L_x + \gamma_xI_x + (1-P_3)t_{2m}I_m, \quad (4)$$

$$\dot{I_s} = \alpha_{ss}\beta_s\frac{L_sI_s}{N} + (1-\lambda_s)\beta_s(\frac{SI_s}{N} + \sigma_s\frac{RI_s}{N}) + \varepsilon_sL_s - (d+\delta_s+t_{2s}+\gamma_s)I_s, \quad (5)$$

$$\dot{I_m} = (1-\lambda_m)\beta_m(\frac{SI_m}{N} + \sigma_m\frac{RI_m}{N} + \alpha_{sm}\frac{L_sI_m}{N}) + \alpha_{mm}\beta_m\frac{L_mI_m}{N} + \varepsilon_mL_m - (d+\delta_m+t_{2m}+\gamma_m)I_m, \quad (6)$$

$$\dot{I_x} = (1-\lambda_x)\beta_x(\frac{SI_x}{N} + \sigma_x\frac{RI_x}{N} + \alpha_{sx}\frac{L_sI_x}{N} + \alpha_{mx}\frac{L_mI_x}{N}) + \alpha_{xx}\beta_x\frac{L_xI_x}{N} + \varepsilon_xL_x - (d+\delta_x+t_{2x}+\gamma_x)I_x, \quad (7)$$

$$\dot{R} = P_1t_{1s}L_s + P_2t_{2s}I_s + P_3t_{2m}I_m + t_{2x}I_x - \sigma_s\beta_s\frac{RI_s}{N} - \sigma_m\beta_m\frac{RI_m}{N} - \sigma_x\beta_x\frac{RI_x}{N} - dR. \quad (8)$$

Also we introduce the list of all parameters and their interpretation in Table 2:

3 Preliminaries and notations

In this section, some basic definitions and properties in the theory of the fractional calculus are presented. Moreover, we introduce the main aspects concerning nonstandard discretization methods.

3.1 Grünwald−Letnikov approximation

We will begin with the signal fractional differential see ([15],[16],[20]),

$$D^\alpha y(t) = f(t,y(t)),\ T \geq t \geq 0,\ and, y(t_0) = 0, \quad (9)$$

where $\alpha > 0$, and D^α denotes the fractional derivative, defined by

$$D^\alpha y(t) = J^{n-\alpha}D^\alpha y(t), \quad (10)$$

where $n-1 < \alpha \leq n,\ n \in N$ and J^n is the nth−order Riemann−Liouville integral operator define as

$$J^n y(t) = \frac{1}{\Gamma(t)}\int_0^t (t-\tau)^{n-1}y(\tau)d\tau,\ with\ \ t > 0, \quad (11)$$

where $\Gamma(\cdot)$ is the gamma function.
To apply Miken's scheme, we have chosen this Grünwald−Letinkov approximation fractional derivative as follows see [11]:

$$D^\alpha y(t) = \lim_{h\to 0} h^{-\alpha}\sum_{j=0}^{[\frac{t}{h}]}(-1)^j\binom{\alpha}{j}y(t-jh) \quad (12)$$

where $[t]$ denote the integer part of t and h is the step size therefore $eq(12)$ is discretized as:

$$\sum_{j=0}^{[\frac{t}{h}]}\omega_j^\alpha y(t_{n-j}) = f(t_n,y(t_n)\quad n = 1,2,3,\cdots. \quad (13)$$

Where $t_n = nh$, and ω_j^α, are the Grünwald−Letnikov coefficients define as
$\omega_j^\alpha = (1-\frac{1+\alpha}{j})\omega_{j-1}^\alpha$ and $\omega_0^\alpha = h^{-\alpha},\ j = 1,2,3,\cdots$

Proposition
Given non negative initial conditions, soluation to (1)-(8) are bounded for all $t \geq 0$. furthermore,the closed set
$C=\{(S,L_s,L_m,L_x,I_s,I_m,I_x,R) \in R_+^8 : S+L_s+L_m+L_x+I_s+I_m+I_x+R \leq \frac{b}{d}\}$, attracts of (1)-(8) for any initial condition in R_+^8.

Table 1: All variables of the system (1)-(8) and their interpretation.

Variable	Definition
$S(t)$	The susceptible population ,individuals who have never encountered TB.
$L_s(t)$	The individuals infected with the drug-sensitive TB strain but who are in a latent stage, $i \cdot e.$, who are neither showing symptoms nor infecting others.
$L_m(t)$	Individuals latently infected with MDR−TB.
$L_x(t)$	Individuals latently infected with XDR−TB.
$I_s(t)$	Individuals infected with the drug-sensitive TB strain who are infectious to others (and most likely, showing symptoms as well).
$I_m(t)$	Those individuals who are infectious with the MDR−TB strain.
$I_x(t)$	Individuals who infectious with the XDR−TB strain.
$R(t)$	Those individuals for whom treatment was successful.
$N(t)$	The total population . $N = S+L_s+L_m+L_x+I_s+I_m+I_x+R.$

Table 2: All parameters in the system (1)-(8) and their interpretation.

Parameter	Interpretation
b	birth/recruitment rate
d	per capita natural death rate
	Disease dynamics
β_r	Transmission coefficient for strain r
λ_r	proportion of newly infected individuals developing $LTBI$ with strain r
$1-\lambda_r$	proportion of newly infected individuals progressing to active TB with strain r due to fast infection
ε_r	per capita rate of endogenous reactivation of L_r
α_{r1}, α_{r2}	proportion of exogenous reinfection of L_{r1} due to contact with I_{r2}
γ_r	per capita rate of natural recovery to the latent stage L_r
δ_r	per capita rate of death due toTB of strain r
	Treatment related
t_{1s}	per capita rate of treatment for L_s
t_{2r}	per capita rate of treatment for I_r. Note that t_{2x} is the rate of successful treatment of $I_x, r \in \{x,m,s\}$
$1-\sigma_r$	Efficiency of treatment in preventing infection with strain r
P_1	probability of treatment success for L_s
$1-P_1$	proportion of treated L_s moved to L_m due to incomplete treatment or lack of strict compliance in the use of drugs
P_2	probability of treatment success for I_s
$1-P_2$	proportion of treated I_s moved to L_m due to incomplete treatment or lack of strict compliance in the use of drugs
P_3	probability of treatment success for I_m
$1-P_3$	proportion of treated I_m moved to $L_x$due to incomplete treatment or lack of strict compliance in the use of drugs

3.2 The basic reproduction number R_0

The basic reproduction number R_0 for system (1)-(8) is given by:

$$R_0 = max(R_{0s}, R_{0m}, R_{0x}), \quad where \tag{14}$$

$$R_{0s} = \frac{\beta_s(\varepsilon_s+(1-\lambda_s)(d+t_{1s}))}{(\varepsilon_s+d+t_{1s})(t_{2s}+\delta_s+d)+\gamma_s(t_{1s}+d)},$$

$$R_{0m} = \frac{\beta_m(\varepsilon_m+(1-\lambda_m)d)}{(\varepsilon_m+d)(t_{2m}+\delta_m+d)+d\gamma_m},$$

$$R_{0x} = \frac{\beta_x(\varepsilon_x+(1-\lambda_x)d)}{(\varepsilon_x+d)(t_{2x}+\delta_x+d)+d\gamma_x}$$

Theorem[2] Asumme that :

$$0 \le \alpha_{ss} \le (1-\lambda_s), \tag{15}$$

$$0 \le \alpha_{mm} \le (1-\lambda_m), \tag{16}$$

$$0 \le \alpha_{xx} \le (1-\lambda_x). \tag{17}$$

Then the disease free equilibrium is globally asymptotically stable when $R_0 < 1$ and endemic equilibria is locally asymptotically stable when $R_0 > 1$.

3.3 NSFD discretization

The nonstandard finite difference schemes were introduced by Mickens in the 1980s as a powerful numerical method that preserves significant properties of exact solutions of the involved differential equation [1]. The concept of the nonstandard finite difference method is discussed in [12].

Definition A numerical scheme is called NSFD discretization if at least one of the following conditions is satisfied [1]:

1.nonlocal approximation is used.

2.the discretization of derivative is not traditional and use a nonnegative function ([12]-[14]).

For the construction of the numerical scheme, concretization of system (1)-(8) are made based on the approximations of temporal derivatives by a generalized forward scheme of first order. Hence, if $f(t) \in C^1(\mathbf{R})$, let us define its derivative as follows:

$$\frac{df(t)}{dt} = \frac{f(t+h)-f(t)}{\varphi(h)} + O(\varphi(h)), \quad as \quad h \to 0, \quad (18)$$

where $\varphi(h)$ is a real-valued function on $\mathbf{R}$. In our work, we will also make use of denominator functions which are little complex functions of the time step-size than the classical one [19]. In addition to this replacement, if there are nonlinear terms such as $\frac{y(t)x(t)}{N(t)}$ in the differential equation, these are replaced by $\frac{y(t+h)x(t)}{N(t)}$ or $\frac{x(t+h)y(t)}{N(t)}$, for more details see ([9],[13]).

Let us denote by S^n, L_s^n, L_m^n, L_x^n, I_s^n, I_m^n, I_x^n and R^n the values of the approximations of $S(nh)$, $L_s(nh)$, $L_m(nh)$, $L_x(nh)$, $I_s(nh)$, $I_m(nh)$, $I_x(nh)$ and $R(nh)$ respectively, for $n = 0,1,2,\cdots$ and h is the timestep of the scheme. The sequences S^n, L_s^n, L_m^n , L_x^n , I_s^n, I_m^n, I_x^n and R^n should be nonnegative in order to be consistent with the biological nature of the model [8].

4 Equilibrium points and their asymptotic stability

Let $\alpha \in (0,1]$ and consider the system (19)-(26)

$$\begin{aligned}
D_t^\alpha S(t) &= f_1(S,L_s,L_m,L_x,I_s,I_m,I_x,R),\\
D_t^\alpha L_s(t) &= f_2(S,L_s,L_m,L_x,I_s,I_m,I_x,R),\\
D_t^\alpha L_m(t) &= f_3(S,L_s,L_m,L_x,I_s,I_m,I_x,R),\\
D_t^\alpha L_x(t) &= f_4(S,L_s,L_m,L_x,I_s,I_m,I_x,R),\\
D_t^\alpha I_s(t) &= f_5(S,L_s,L_m,L_x,I_s,I_m,I_x,R),\\
D_t^\alpha I_m(t) &= f_6(S,L_s,L_m,L_x,I_s,I_m,I_x,R),\\
D_t^\alpha I_x(t) &= f_7(S,L_s,L_m,L_x,I_s,I_m,I_x,R),\\
D_t^\alpha R(t) &= f_8(S,L_s,L_m,L_x,I_s,I_m,I_x,R).
\end{aligned}$$

With the initial values $(S(0), L_s(0), L_m(0), L_x(0), I_s(0), I_m(0), I_x(0), R(0))$. To evaluate the equilibrium point let

$D_t^\alpha S = D_t^\alpha L_s = D_t^\alpha L_m = D_t^\alpha L_x = D_t^\alpha I_s = D_t^\alpha I_m = D_t^\alpha I_x = D_t^\alpha R = 0$

$\Rightarrow f_i(S^{eq},L_s^{eq},L_m^{eq},L_x^{eq},I_s^{eq},I_m^{eq},I_x^{eq},R^{eq}) = 0, \ \ i = 1,2,3,...,8.$

from which we can get the equilibrium points $(S^{eq},L_s^{eq},L_m^{eq},L_x^{eq},I_s^{eq},I_m^{eq},I_x^{eq},R^{eq})$. To evaluate the asymptotic stability let

$$\begin{aligned}
S(t) &= S^{eq} + \varepsilon_1(t),\\
L_s(t) &= L_s^{eq}(t) + \varepsilon_2(t),\\
L_m(t) &= L_m^{eq}(t) + \varepsilon_3(t),\\
L_x(t) &= L_x^{eq}(t) + \varepsilon_4(t),\\
I_s(t) &= I_s^{eq}(t) + \varepsilon_5(t),\\
I_m(t) &= I_m^{eq}(t) + \varepsilon_6(t),\\
I_x(t) &= I_x^{eq}(t) + \varepsilon_7(t),\\
R(t) &= R^{eq} + \varepsilon_8(t).
\end{aligned}$$

So the equilibrium point (S^{eq}, L_s^{eq}, L_m^{eq}, L_x^{eq}, I_s^{eq}, I_m^{eq}, I_x^{eq}, R^{eq}) is locally asymptotically stable if all eignvalues of Jacobian evaluated at the equilibrium point satisfies

$$|arg\lambda_i| > \frac{\alpha\pi}{2}, \quad where \ \ i = 1,2,....,8 \quad ([6],[10])$$

5 Fractional−order derivatives for multi−strain TB model

In the following, we introduce the fraction order multi-strain TB model, the new system is described by fractional order differential equations:

$$D_t^\alpha S = b - dS - \beta_s\frac{SI_s}{N} - \beta_m\frac{SI_m}{N} - \beta_x\frac{SI_x}{N}, \quad (19)$$

$$\begin{aligned}
D_t^\alpha L_s =& \lambda_s\beta_s\frac{SI_s}{N} + \sigma_s\lambda_s\beta_s\frac{RI_s}{N} - \alpha_{ss}\beta_s\frac{L_sI_s}{N}\\
&- \alpha_{sm}\beta_m\frac{L_sI_m}{N} - \alpha_{sx}\beta_x\frac{L_sI_x}{N}\\
&- (d+\varepsilon_s+t_{1s})L_s + \gamma_sI_s, \quad (20)
\end{aligned}$$

$$\begin{aligned}
D_t^\alpha L_m =& \lambda_m\beta_m\frac{SI_m}{N} + \sigma_m\lambda_m\beta_m\frac{RI_m}{N} + \alpha_{sm}\beta_m\lambda_m\frac{L_sI_m}{N}\\
&- \alpha_{mm}\beta_m\frac{L_mI_m}{N} - \alpha_{mx}\beta_x\frac{L_mI_x}{N} - (d+\varepsilon_m)L_m\\
&+ (1-P_1)t_{1s}L_s + (1-P_2)t_{2s}I_s + \gamma_mI_m, \quad (21)
\end{aligned}$$

$$\begin{aligned}
D_t^\alpha L_x =& \lambda_x\beta_x\frac{SI_x}{N} + \sigma_x\lambda_x\beta_x\frac{RI_x}{N} + \alpha_{sx}\beta_x\lambda_x\frac{L_sI_x}{N}\\
&+ \alpha_{mx}\beta_x\lambda_x\frac{L_mI_x}{N} + (1-P_3)t_{2m}I_m\\
&- \alpha_{xx}\beta_x\frac{L_xI_x}{N} - (d+\varepsilon_x)L_x + \gamma_xI_x, \quad (22)
\end{aligned}$$

$$\begin{aligned}
D_t^\alpha I_s =& \alpha_{ss}\beta_s\frac{L_sI_s}{N} + (1-\lambda_s)\beta_s(\frac{SI_s}{N} + \sigma_s\frac{RI_s}{N})\\
&+ \varepsilon_sL_s - (d+\delta_s+t_{2s}+\gamma_s)I_s, \quad (23)
\end{aligned}$$

$$D_t^\alpha I_m = \alpha_{mm}\beta_m\frac{L_mI_m}{N} + (1-\lambda_m)\beta_m(\frac{SI_m}{N} + \sigma_m\frac{RI_m}{N})$$

$$+(1-\lambda_m)\beta_m\alpha_{sm}\frac{L_sI_m}{N}+\varepsilon_mL_m$$
$$-(d+\delta_m+t_{2m}+\gamma_m)I_m, \quad (24)$$

$$D_t^\alpha I_x=\alpha_{xx}\beta_x\frac{L_xI_x}{N}+(1-\lambda_x)\beta_x(\frac{SI_x}{N}+\sigma_x\frac{RI_x}{N}+\alpha_{sx}\frac{L_sI_x}{N})$$
$$+(1-\lambda_x)\beta_x\alpha_{mx}\frac{L_mI_x}{N}+\varepsilon_xL_x$$
$$-(d+\delta_x+t_{2x}+\gamma_x)I_x, \quad (25)$$

$$D_t^\alpha R=P_1t_{1s}L_s+P_2t_{2s}I_s+P_3t_{2m}I_m+t_{2x}I_x-\sigma_s\beta_s\frac{RI_s}{N}$$
$$-\sigma_m\beta_m\frac{RI_m}{N}-\sigma_x\beta_x\frac{RI_x}{N}-dR. \quad (26)$$

where D_t^α is the Caputo fractional derivative. Because model (19)-(26) monitors the dynamics of human populations, all the parameters are assumed to be nonnegative. To evaluate the equilibrium points:

Let $D_t^\alpha S=D_t^\alpha L_s=D_t^\alpha L_m=D_t^\alpha L_x=D_t^\alpha I_s=D_t^\alpha I_m=D_t^\alpha I_x=D_t^\alpha R=0$

$\Rightarrow \quad f_i(S^{eq},L_s^{eq},L_m^{eq},L_x^{eq},I_s^{eq},I_m^{eq},I_x^{eq},R^{eq})=0$, i=1,2,3,...,8.

Now, if $I_s(t)=I_m(t)=I_x(t)=0\Rightarrow L_s(t)=L_m(t)=L_x(t)=0$, $R(t)=0$ and $S(t)=\frac{b}{d}$.

Then DFE is $E_0=\{(\frac{b}{d},0,0,0,0,0,0,0)\}$.
We calculate the Jacobian matrix of the system (1)-(8) at DFE point as following:

$$J(E_0)=\begin{pmatrix} a&0&0&0&b&c&d_1&0\\ 0&e&0&0&f&0&0&0\\ 0&g&h&0&p&q&0&0\\ 0&0&0&r&0&s&t&0\\ 0&u&0&0&v&0&0&0\\ 0&0&w&0&0&x&0&0\\ 0&0&0&y&0&0&z&0\\ 0&m&0&0&n&j&k&a \end{pmatrix},$$

where $a=-d$, $b=-\beta_s$, $c=-\beta_m$, $d_1=-\beta_x$, $e=-(d+\varepsilon_s+t_{1s})$, $f=\gamma_s+\lambda_s\beta_s$, $g=(1-p_1)t_{1s}$, $h=-(d+\varepsilon_m)$, $p=(1-p_2)t_{2s}$, $q=\gamma_m+\lambda_m\beta_m$, $r=-(d+\varepsilon_x)$, $s=(1-p_3)t_{2m}$, $t=\gamma_x+\lambda_x\beta_x$, $u=\varepsilon_s$, $v=-(d+\delta_s+t_{2s}+\gamma_s)$, $w=\varepsilon_m$, $x=-(d+\delta_m+t_{2m}+\gamma_m)$, $y=\varepsilon_x$, $z=-(d+\delta_x+t_{2x}+\gamma_x)$, $m=p_1t_{1s}$, $n=p_2t_{2s}$, $j=p_3t_{2m}$, $k=t_{2x}$.

The characteristic equation associated with above matrix is $|J(E_0)-\lambda I|=0\Rightarrow$
$(a-\lambda)^2(\lambda^2-(r+z)\lambda-yt+zr)(-\lambda^2+(h+x)\lambda-xh+wq)(-\lambda^2+(e+v)\lambda+uf-ve)=0$. Then the eigenvalues of Jacobian matrix are $\lambda_{1,2}=-d$, $\lambda_{3,4}=\frac{r+z\pm\sqrt{(r^2-2zr+z^2+4yt)}}{2}$, $\lambda_{5,6}=\frac{x+h\pm\sqrt{(x^2-2xh+h^2+4wq)}}{2}$, $\lambda_{7,8}=\frac{v+e\pm\sqrt{(v^2-2ve+e^2+4uf)}}{2}$, by using Theorem (Routh Hurwitz Criteria), these roots are negative or have negative real parts and DFE is locally asymptotically stable if all eigenvalues of the Jacobian matrix satisfies Matignon's conditions given by $(|arg\lambda_i|>\frac{\alpha\pi}{2})$.

For simplicity, we will determine the stability of DFE numerically by using Table 3 and put $\beta_s=\beta_m=\beta_x=0.1$. Then eigenvalues are $\lambda_1=-0.3800$, $\lambda_2=-0.3800$, $\lambda_3=-0.3675$, $\lambda_4=-0.3675$, $\lambda_5=-1.2215$, $\lambda_6=-1.2215$, $\lambda_7=-2.0882$, $\lambda_8=-1.2268$. So, if $R_0<1$, DFE is locally asymptotically stable since $|arg\lambda_i|=|-\pi|>\frac{\alpha\pi}{2}$.

If at least one of the infected variables is non-zero, then the solution correspond to the endemic equilibrium for model (19)-(26). This system is highly nonlinear in I_s, I_m and I_x, and hence explicit solution are not obtainable. So we solve the system (19)-(26) numerically to obtain endemic fixed point.

5.1 NSFD for fractional differential equations

The system (19)-(26) can be discretized as follows:

$$\sum_{j=0}^{n+1}\omega_j^\alpha S^{n+1-j}=b-dS^{n+1}-\beta_s\frac{S^{n+1}I_s^n}{N^n}-\beta_m\frac{S^{n+1}I_m^n}{N^n}$$
$$-\beta_x\frac{S^{n+1}I_x^n}{N^n}, \quad (27)$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha L_s^{n+1-j}=\lambda_s\beta_s\frac{S^{n+1}I_s^n}{N^n}+\sigma_s\lambda_s\beta_s\frac{R^{n+1}I_s^n}{N^n}+\gamma_sI_s^n$$
$$-\alpha_{ss}\beta_s\frac{L_s^{n+1}I_s^n}{N^n}-\alpha_{sx}\beta_x\frac{L_s^{n+1}I_x^n}{N^n}$$
$$-\alpha_{sm}\beta_m\frac{L_s^{n+1}I_m^n}{N^n}-(d+\varepsilon_s+t_{1s})L_s^{n+1}, \quad (28)$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha L_m^{n+1-j}=\lambda_m\beta_m\frac{S^{n+1}I_m^n}{N^n}+\sigma_m\lambda_m\beta_m\frac{R^{n+1}I_m^n}{N^n}$$
$$+\lambda_m\alpha_{sm}\beta_m\frac{L_s^{n+1}I_m^n}{N^n}+t_{1s}L_s^{n+1}-P_1t_{1s}L_s^{n+1}$$
$$+t_{2s}I_s^n-P_2t_{2s}I_s^n-\alpha_{mm}\beta_m\frac{L_m^{n+1}I_m^n}{N^n}$$
$$+\gamma_mI_m^n-\alpha_{mx}\beta_x\frac{L_m^{n+1}I_x^n}{N^n}-(d+\varepsilon_m)L_m^{n+1}, \quad (29)$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha L_x^{n+1-j}=\lambda_x\beta_x\frac{S^{n+1}I_x^n}{N^n}+\sigma_x\lambda_x\beta_x\frac{R^{n+1}I_x^n}{N^n}$$
$$+\lambda_x\alpha_{sx}\beta_x\frac{L_s^{n+1}I_x^n}{N^n}+\lambda_x\alpha_{mx}\beta_x\frac{L_m^{n+1}I_x^n}{N^n}$$
$$+t_{2m}I_m^n-P_3t_{2m}I_m^n-\alpha_{xx}\beta_x\frac{L_x^{n+1}I_x^n}{N^n}$$
$$+\gamma_xI_x^n-(d+\varepsilon_x)L_x^{n+1}, \quad (30)$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha I_s^{n+1-j}=(1-\lambda_s)\beta_s(\frac{S^{n+1}I_s^n}{N^n}+\sigma_s\frac{R^{n+1}I_s^n}{N^n})$$

Table 3: All parameters in the system (1)-(8) and the reference of the parameters.

parameter	value	Reference
b	3190	Assumed
d	0.38	[18]
$\beta_s=\beta_m=\beta_x$	14	[18]
$\lambda_s=\lambda_m=\lambda_x$	0.5	Assumed
$\varepsilon_s=\varepsilon_m=\varepsilon_x$	0.5	Assumed
$\alpha_{r1,r2}$	0.05	Assumed
$\gamma_s=\gamma_m=\gamma_x$	0.3	Assumed
t_{1s}	0.88	[18]
$t_{2r}: r\in(s,m,x)$	$t_{2s}=0.88; t_{2m}=t_{2x}=0.034$	[18]
σ_r	0.25	[18]
P_r	0.88	[18]
δ_r	0.045	[18]

$$+\alpha_{ss}\beta_s\frac{L_s^{n+1}I_s^n}{N^n}+\varepsilon_s L_s^{n+1}$$
$$-(d+\delta_s)I_s^{n+1}-(\gamma_s+t_{2s})I_s^n, \tag{31}$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha I_m^{n+1-j}=(1-\lambda_m)\beta_m\left(\frac{S^{n+1}I_m^n}{N^n}+\sigma_m\frac{R^{n+1}I_m^n}{N^n}\right)$$
$$+\alpha_{mm}\beta_m\frac{L_m^{n+1}I_m^n}{N^n}+(1-\lambda_m)\beta_m\alpha_{sm}\frac{L_s^{n+1}I_m^n}{N^n}$$
$$+\varepsilon_m L_m^{n+1}-(d+\delta_m)I_m^{n+1}$$
$$-(\gamma_m+t_{2m})I_m^n, \tag{32}$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha I_x^{n+1-j}=(1-\lambda_x)\beta_m\left(\frac{S^{n+1}I_x^n}{N^n}+\sigma_x\frac{R^{n+1}I_x^n}{N^n}\right)$$
$$+\alpha_{xx}\beta_x\frac{L_x^{n+1}I_x^n}{N^n}+(1-\lambda_x)\beta_m\alpha_{mx}\frac{L_x^{n+1}I_m^n}{N^n}$$
$$+\varepsilon_x L_x^{n+1}-(d+\delta_x)I_x^{n+1}-(\gamma_x+t_{2x})I_x^n, \tag{33}$$

$$\sum_{j=0}^{n+1}\omega_j^\alpha R^{n+1-j}=P_1t_{1s}L_s^{n+1}+P_2t_{2s}I_s^n+P_3t_{2m}I_m^n+t_{2x}I_x^n$$
$$-\sigma_s\beta_s\frac{R^{n+1}I_s^n}{N^n}-\sigma_m\beta_m\frac{R^{n+1}I_m^n}{N^n}$$
$$-\sigma_x\beta_x\frac{R^{n+1}I_x^n}{N^n}-dR^{n+1}. \tag{34}$$

where the discretizations for $N(t)$ is given as:

$$N^n=S^n+L_s^n+L_m^n+L_x^n+I_s^n+I_m^n+I_x^n+R^n.$$

And $\omega_0^\alpha=(\varphi_i(h))^{-\alpha},\ i=1,2,\cdots,8$. Where, the nonlocal approximations are used for the nonlinear terms and the following denominator functions are used:

$$\varphi_1(h)=\frac{e^{dh}-1}{d},\qquad \varphi_2(h)=\frac{e^{(d+\varepsilon_s+t_{1s})h}-1}{(d+\varepsilon_s+t_{1s})},$$
$$\varphi_3(h)=\frac{e^{(d+\varepsilon_m)h}-1}{(d+\varepsilon_m)},\quad \varphi_4(h)=\frac{e^{(d+\varepsilon_x)h}-1}{(d+\varepsilon_x)},$$
$$\varphi_5(h)=\frac{1-e^{-(d+\delta_s)h}}{(\gamma_s+t_{2s})},\quad \varphi_6(h)=\frac{1-e^{-(d+\delta_m)h}}{(\gamma_m+t_{2m})},$$
$$\varphi_7(h)=\frac{1-e^{-(d+\delta_x)h}}{(\gamma_x+t_{2x})},\quad \varphi_8(h)=\frac{e^{dh}-1}{d}.$$

We obtain,

$$S^{n+1}=\frac{b-\sum_{j=1}^{n+1}\omega_j^\alpha S^{n+1-j}}{(\varphi_1(h))^{-\alpha}+d+\frac{\beta_s I_s^n+\beta_m I_m^n+\beta_x I_x^n}{N^n}}, \tag{35}$$

$$L_s^{n+1}=\frac{\frac{\beta_s I_s^n}{N^n}\lambda_s(S^{n+1}+\sigma_s R^{n+1})+\gamma_s I_s^n}{(\varphi_2(h))^{-\alpha}+(d+t_{1s}+\varepsilon_s)+\frac{1}{N^n}(\alpha_{ss}\beta_s I_s^n+\alpha_{sm}\beta_m I_m^n+\alpha_{sx}\beta_x I_x)}$$
$$-\frac{\sum_{j=1}^{n+1}\omega_j^\alpha L_s^{n+1-j}}{(\varphi_2(h))^{-\alpha}+(d+t_{1s}+\varepsilon_s)+\frac{1}{N^n}(\alpha_{ss}\beta_s I_s^n+\alpha_{sm}\beta_m I_m^n+\alpha_{sx}\beta_x I_x)} \tag{36}$$

$$L_m^{n+1}=\frac{\frac{\beta_m\lambda_m I_m^n}{N^n}(S^{n+1}+\sigma_m R^{n+1}+\alpha_{sm}L_s^{n+1})+\gamma_m I_m^n+t_{1s}L_s^{n+1}(1-P_1)}{(\varphi_3(h))^{-\alpha}+(d+\varepsilon_m)+\frac{1}{N^n}(\alpha_{mm}\beta_m I_m^n+\alpha_{mx}\beta_x I_x^n)}$$
$$+\frac{t_{2s}I_s^n(1-P_2)-\sum_{j=1}^{n+1}\omega_j^\alpha L_m^{n+1-j}}{(\varphi_3(h))^{-\alpha}+(d+\varepsilon_m)+\frac{1}{N^n}(\alpha_{mm}\beta_m I_m^n+\alpha_{mx}\beta_x I_x^n)}, \tag{37}$$

$$L_x^{n+1}=\frac{\frac{\beta_x\lambda_x I_x^n}{N^n}(S^{n+1}+\sigma_x R^{n+1}+\alpha_{sx}L_s^{n+1}+\alpha_{mx}L_m^{n+1})+t_{2s}I_m^n(1-P_3)}{(\varphi_4(h))^{-\alpha}+(d+\varepsilon_x)+\frac{1}{N^n}(\alpha_{xx}\beta_x I_x^n)}$$
$$+\frac{\gamma_x I_x^n-\sum_{j=1}^{n+1}\omega_j^\alpha L_x^{n+1-j}}{(\varphi_4(h))^{-\alpha}+(d+\varepsilon_x)+\frac{1}{N^n}(\alpha_{xx}\beta_x I_x^n)}, \tag{38}$$

$$I_s^{n+1}=\frac{\varphi_5(h)\beta_s\frac{I_s^n}{N^n}(\alpha_{ss}L_s^{n+1}+(1-\lambda_s)(S^{n+1}+\sigma_s R^{n+1}))}{(\varphi_5(h))^{-\alpha}+(d+\delta_s)}$$
$$-\frac{(\gamma_s+(t_{2s}))I_s^n+\varepsilon_s L_s^{n+1}-\sum_{j=1}^{n+1}\omega_j^\alpha I_s^{n+1-j}}{(\varphi_5(h))^{-\alpha}+(d+\delta_s)}, \tag{39}$$

$$I_m^{n+1}=\frac{\beta_m\frac{I_m^n}{N^n}(\alpha_{mm}L_m^{n+1}+(1-\lambda_m)(S^{n+1}+\sigma_m R^{n+1}+\alpha_{sm}L_s^{n+1}))}{(\varphi_6(h))^{-\alpha}+(d+\delta_m)}$$
$$-\frac{(\gamma_m+(t_{2m}))I_m^n+\varepsilon_m L_m^{n+1}-\sum_{j=1}^{n+1}\omega_j^\alpha I_m^{n+1-j}}{(\varphi_6(h))^{-\alpha}+(d+\delta_m)}, \tag{40}$$

$$I_x^{n+1} = \frac{\beta_x \frac{I_x^n}{N^n}(\alpha_{xx}L_x^{n+1}+(1-\lambda_x)(S^{n+1}+\sigma_x R^{n+1}+\alpha_{sx}L_s^{n+1}+\alpha_{mx}L_m^{n+1}))}{(\varphi_7(h))^{-\alpha}+(d+\delta_x)} - \frac{(\gamma_x+(t_{2x}))I_x^n+\varepsilon_x L_x^{n+1}-\sum_{j=1}^{n+1}\omega_j^\alpha I_x^{n+1-j}}{(\varphi_7(h))^{-\alpha}+(d+\delta_x)}, \quad (41)$$

$$R^{n+1} = \frac{t_{1s}P_1L_s^{n+1}+P_2t_{2s}I_s^n+t_{2m}P_3I_m^n+t_{2x}I_x^n-\sum_{j=1}^{n+1}\omega_j^\alpha R^{n+1-j}}{(\varphi_8(h))^{-\alpha}+d+\frac{1}{N^n}(\sigma_s\beta_sI_s^n+\sigma_m\beta_mI_m^n+\sigma_x\beta_xI_x^n)}. \quad (42)$$

6 Numerical results and simulations

Since most of the fractional−order differential equations do not have exact analytic solutions, so approximation and numerical techniques must be used. Several analytical and numerical methods have been proposed to solve the fractional-order differential equations. For numerical solutions of the system (19)-(26) one can use the nonstandard finite difference method, the approximate solution $S(t)$, $L_s(t)$, $L_m(t)$, $L_x(t)$, $I_s(t)$, $I_m(t)$, $I_x(t)$, $R(t)$ are display in Figure 1, when $R_0 < 1$ and Figure 2 when $R_0 > 1$, in each Figure three different values of $\alpha = 1, \alpha = 0.5, \alpha = 0.8$ are considered and the endemic equilibrium is locally asympototically stable, for example we consider $\beta_s = \beta_m = \beta_x = 14$ and $\alpha = 0.8$, with initial value $S(0)$, $L_s(0)$, $L_m(0)$, $L_x(0)$, $I_s(0)$, $I_m(0)$, $I_x(0)$, $R(0)$ = $(5000, 50, 50, 50, 30, 30, 30, 60)$, the approximate solutions are displayed in Figure 3 the endemic equilibrium of NSFDM is locally asympototically stable where the eigenvalues given as λ_1=−9.1156, λ_2=−0.4141, λ_3=−0.1499, λ_4=−2.6366, λ_5=−1.4130, λ_6=−1.6031, λ_7=−1.0045, λ_8=−2.4750. Then $|arg\lambda_i| = |-\pi| > \frac{\alpha\pi}{2}$. When $\alpha = 1$, system (19)-(26) is the classical integer-order system (1)-(8). Moreover, we report in Table 4 the convergence behavior of numerical methods to the disease free equilibrium, and in Table 5 report the convergence behavior of numerical methods to the endemic equilibrium. In Figure 3, present the result obtained by NSFDM and SFDM with step size $h = 0.1$ and $\alpha = 0.8$. We can clearly see, all schemes converge to correct endemic equilibrium. Previous Figures $4(a-d)$ illustrate propagation of TB along the time when $\alpha = 0.8$ as following:

–In Figure 4*a*, the relationship between $R(t)$ and $I_s(t)$ illustrate that, there are individuals succeeded treatment with them, may are exposed to infection again by contagious members $I_s(t)$ of the first strain . At the beginning of the period of the time the number of $I_s(t)$ members are increases and the number of $R(t)$ members are decreases, then after time steps the curves are intersect again and $I_s(t)$ will be response to treatment and their numbers will be decreases.

–In Figure 4*b*, the relationship between $S(t)$ and $I_x(t)$, describes the spread of infection from the members of the third strain to healthy people, then the number of infectious people will be increases and the number of healthy people are decreases with proper time.

–In Figure 4*c*, the relationship between $S(t)$ and $I_m(t)$, describes the spread of contagious from the members $I_m(t)$ of the second strian to healthy people, then the number of infectious people will be increases and the number of healthy people are decreases with proper time.

–In Figure 4*d*, the relationship between $L_s(t)$ and $I_s(t)$, describes the spread of contagious from the members $I_s(t)$ of the first strain to individuals who carry the disease latent of the first strain $L_s(t)$, after time steps the curves are intersect agian then $I_s(t)$ will be response to treatment and the number of them are decreases.

In Figure 5, we present the results obtained by using NSFDM and SFDM with step size $h = 1$, and $\alpha = 0.8$. As we can clearly see, the SFDM is unstable and the solutions are divergent. from Table 4, we can conclude

Table 4: Result obtained by SFDM and NSFDM for $B_s = B_m = B_x = 0.1$, $R_0 < 1$, $\alpha = 0.8$, and initial conditions as $(5000, 50, 50, 50, 30, 30, 30, 60)$ with different time step size.

h	SFDM	NSFDM
0.01	convergent	convergent
0.1	convergent	convergent
1	convergent	convergent
20	divergent	convergent
100	divergent	convergent

Table 5: Result obtained by using SFDM and NSFDM for $B_s = B_m = B_x = 14$, $R_0 > 1$, $\alpha = 0.8$, and initial conditions as $(5000, 50, 50, 50, 30, 30, 30, 60)$ with different time step size.

h	SFDM	NSFDM
0.01	convergent	convergent
0.1	convergent	convergent
1	divergent	convergent
20	divergent	convergent
100	divergent	convergent

that NSFDM is unconditionally converge to the correct disease free equilibria for large h, while the SFDM converge only when h is small.
from Table 5, we can conclude that NSFDM is unconditionally converge to the correct endemic equilibria for large h, while the SFDM converge only when h is small. Moreover, the system (27)-(34)is unconditionally locally asymptotically stable.
Moreover, from these numerical results obtained in this work we can control the disease and turn the endemic point to the disease free point as follows:

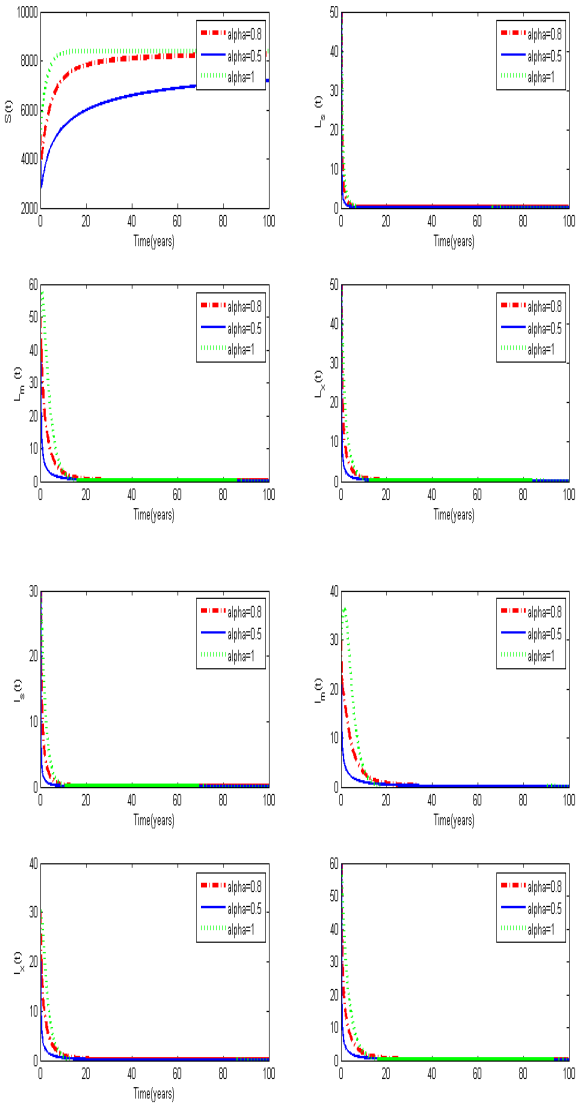

Fig. 1: Profiles obtained by using NSFD method with different α and $h = 0.1$, $\beta_s = \beta_m = \beta_x = 0.1$, $R_0 < 1$.

Let us consider,

$$R_{0s} < 1 \Rightarrow \frac{-t_{2s}^2 + 5.3950t_{2s} + 8.6060}{t_{2s}^2 + 1.6050t_{2s} + 1.050} < 0, \text{where } t_{1s} = t_{2s}. \tag{43}$$

$$R_{0m} < 1 \Rightarrow \frac{9.1720 - 0.8800t_{2m}}{0.8800t_{2m} + 0.4880} < 0, \tag{44}$$

$$R_{0x} < 1 \Rightarrow \frac{9.1720 - 0.8800t_{2x}}{0.8800t_{2x} + 0.4880} < 0. \tag{45}$$

Then $t_{1s} = t_{2s} \geq 6.6828, t_{2m} \geq 10.4227, t_{2x} \geq 10.4227.$ (46)

$$T = max\{t_{2s} \geq 6.6828, t_{2m} \geq 10.4227, t_{2x} \geq 10.4227\},$$

$$\Rightarrow T = t_{2m} = t_{2x} \geq 10.4227. \tag{47}$$

Then, if we choose the following elements which belongs to T : $t_{2s} = t_{2m} = t_{2x} = 15$, and $B_s = B_m = B_x = 14$, h=2, $\alpha = 0.8$ see Figure 6.

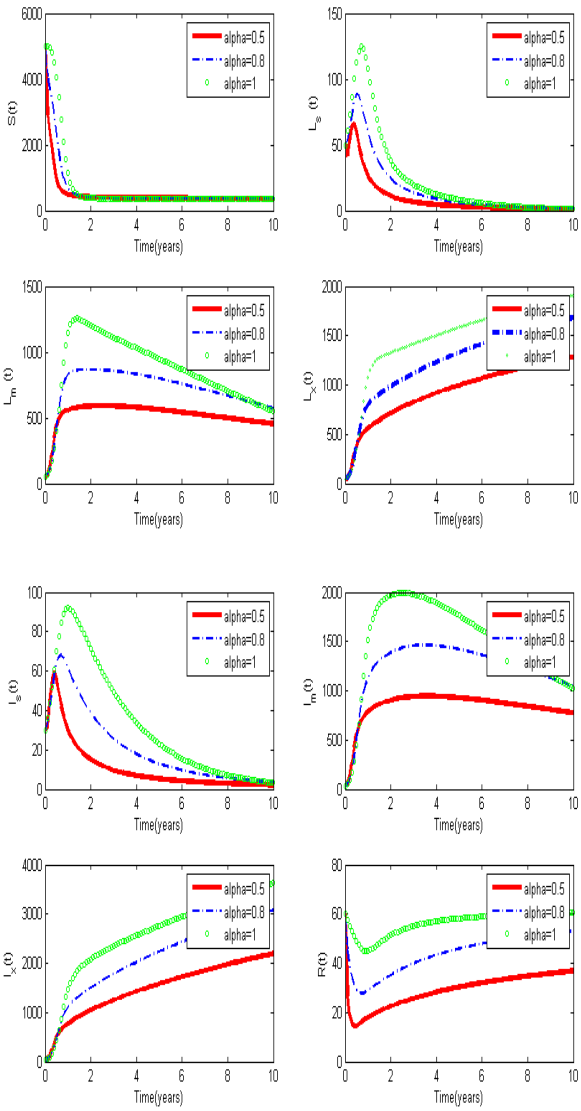

Fig. 2: Profiles obtained by using NSFD method with different α and $h = 0.1$, $\beta_s = \beta_m = \beta_x = 14$, and $R_0 > 1$.

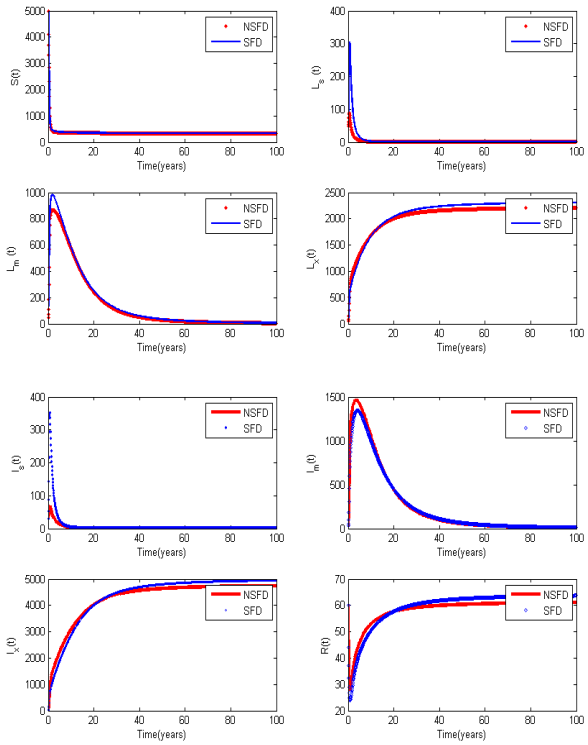

Fig. 3: Profiles obtained by using NSFD and SFD methods with $\alpha = 0.8$, $h = 0.1$, $\beta_s = \beta_m = \beta_x = 14$, and $R_0 > 1$.

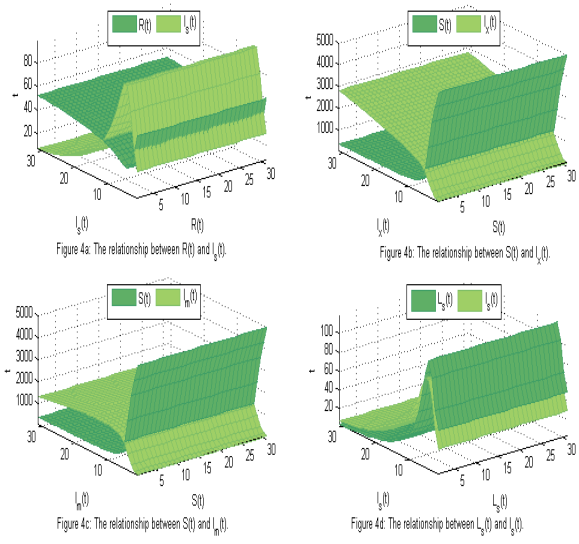

Fig. 4: Illustrate propagation of multi−strain TB along the time when $\alpha = 0.8$, $h = 0.3$, $\beta_s = \beta_m = \beta_x = 14$, and $R_0 > 1$, by using NSFDM.

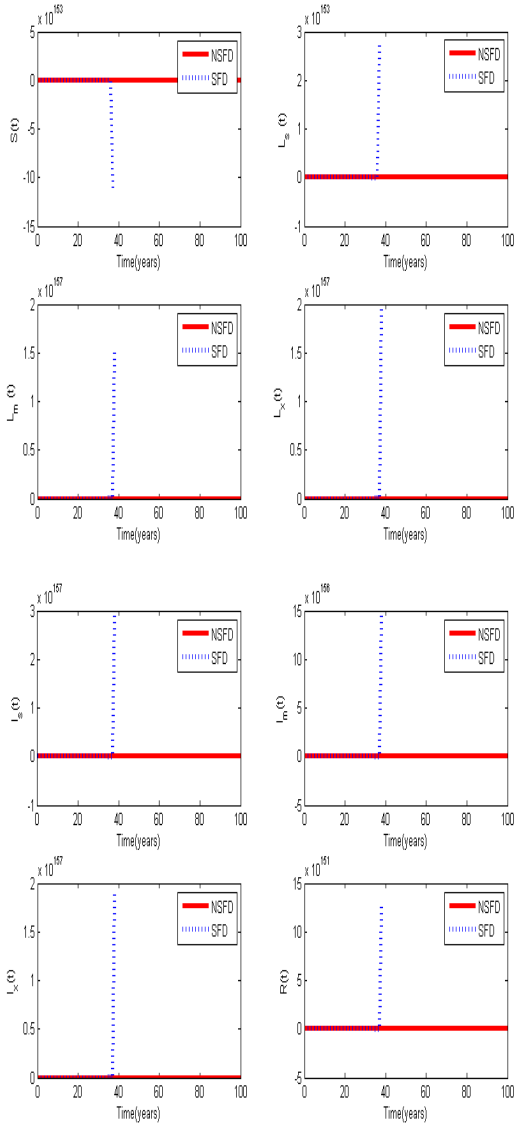

Fig. 5: Profiles obtained by using NSFD and SFD methods with $\alpha = 0.8$, $h = 1$, $\beta_s = \beta_m = \beta_x = 14$, and $R_0 > 1$.

7 Conclusions

In this paper, the multi−strain TB model of fractional order derivatives which incorporates three strains: drug−sensitive, MDR and XDR is studied. The model we considered here included several factors of spreading TB such as the fast infection, the exogenous reinfection and secondary infection along with the resistance factor. It can be concluded from the numerical results presented in this paper, that the fractional order model for TB, is generalization and more suitable than integer order. Moreover, NSFD scheme considered here is more efficient for solving fractional order model for

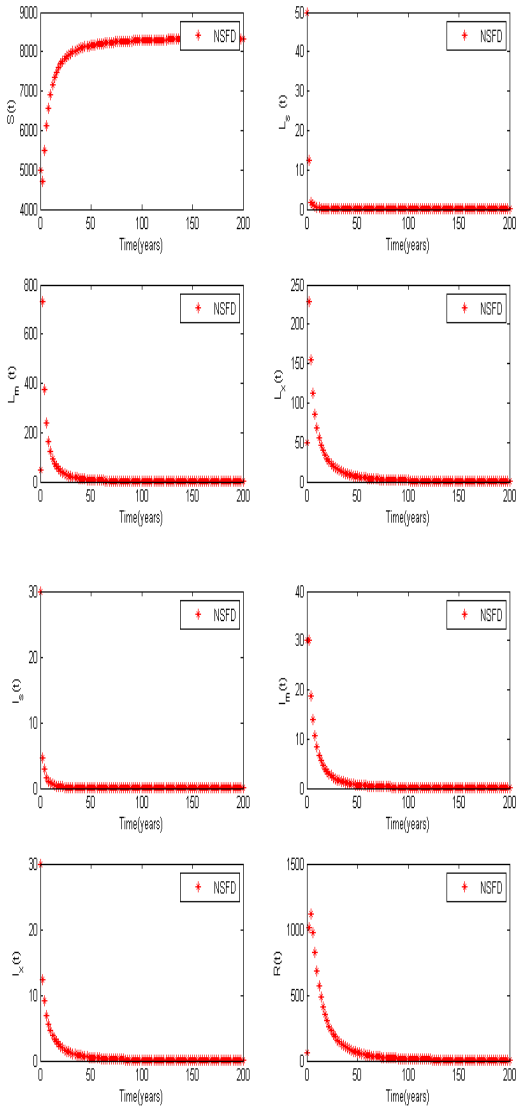

Fig. 6: Profiles obtained by using NSFD for $h = 2$, $\alpha = 0.8$, $\beta_s = \beta_m = \beta_x = 14$, $t_{2s} = t_{2m} = t_{2x} = 15$.

multi−strain TB, than SFD scheme. It preserves the positivity of the solution, and the stability regions are larger than SFD method.

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