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A Fractional Measles Model Having Monotonic Real Statistical Data for Constant Transmission Rate of the Disease

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Abstract: Non-Markovian effects have a vital role in modeling the processes related with natural phenomena such as epidemiology. Various infectious diseases have long-range memory characteristics and, thus, non-local operators are one of the best choices to be used to understand the transmission dynamics of such diseases and epidemics. In this paper, we study a fractional order epidemiological model of measles. Some relevant features, such as well-posedness and stability of the underlying Cauchy problem, are considered accompanying the proofs for a locally asymptotically stable equilibrium point for basic reproduction number $\mathcal{R}_0 < 1$, which is most sensitive to the fractional order parameter and to the percentage of vaccination. We show the efficiency of the model through a real life application of the spread of the epidemic in Pakistan, comparing the fractional and classical models, while assuming constant transmission rate of the epidemic with monotonically increasing and decreasing behavior of the infected population. Secondly, the fractional Caputo type model, based upon nonlinear least squares curve fitting technique, is found to have smaller residuals when compared with the classical model.

Keywords: non-integer calculus; epidemiological models; numerical simulations

1. Introduction

Diseases are very much around and the burden for some of the infectious diseases has always remained substantially high in human society. Diseases, such as smallpox, rubella, mumps, cholera, measles, black plague, HIV/AIDS, malaria, influenza, Ebola, among others, keep epidemiologists, ecologist, applied mathematicians, and statisticians altogether busy in mathematical modeling of these infectious diseases. Epidemiological models are an important tool for health organizations, since they provide information on the spread of diseases and allow the choice of the best strategies to deal with them. Since the pioneering works of Kermack and McKendrick [1–3], numerous works on this subject have arisen to study the dynamics of the spread of different diseases.

However, various researchers are concerned with the design of mathematical epidemiological models with the tools taken from standard classical calculus, where one is restricted to use only integer-order derivatives. On the other hand, classical epidemiological models when studied in the domain of fractional calculus, wherein infinite degrees of freedom are available for the order of differentiation, are proven to have better capability to capture the more accurate behavior for the transmission dynamics of the epidemic under consideration while yielding comparatively smaller amount of error associated with the nonlinear parameter estimation (see, e.g., [4–10]).

One of those concerns is the behavior of measles propagation among human society. Despite much progress in the development of new vaccines for the elimination and eradication of infectious diseases, the disease of measles is still commonly found in many parts of the world. Anyone who is not protected, through vaccination or past infection, is at risk of getting the disease, especially when traveling abroad and thus putting many people (babies, in particular) at risk.

Motivated by the epidemiological model presented in [11], where a system of first order ordinary differential equations (ODEs) is introduced to model measles transmission, we study its fractional extension in the present research work. Each first order derivative x' is replaced by the Caputo fractional derivative of order $\alpha \in (0,1)$ [12]:

$$ {}^{C}D^{\alpha}_{0+}x(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t (t-\tau)^{-\alpha} x'(\tau) d\tau, \quad t > 0, $$

where $x : [0, b] \to \mathbb{R}$ is a given function and Γ denotes the Gamma function. Also, to ensure that both sides of the fractional differential equation have the same dimension, each dimensional parameter p is replaced by p^{α} (see [13] for an explanation). The parameters of the model are displayed in the Table 1.

Table 1. Parameters of the measles model.

β	disease transmission rate	Estimated
A	birth rate	Fixed
μ	natural mortality rate	Fixed
ρ	percentage of vaccinated individuals	Fixed
σ	rate at which an exposed person becomes infective	Fixed
γ	rate an infected recovers	Fixed
α	fractional order parameter	Estimated

The fractional version of the measles model with constant transmission rate $\beta > 0$ of the infection is proposed as follows.

$$ \begin{cases} {}^{C}D^{\alpha}_{0+}S &= A^{\alpha}(1-\rho) - \beta^{\alpha} IS - \mu^{\alpha} S \\ {}^{C}D^{\alpha}_{0+}E &= \beta^{\alpha} IS - (\sigma^{\alpha} + \mu^{\alpha})E \\ {}^{C}D^{\alpha}_{0+}I &= \sigma^{\alpha} E - (\gamma^{\alpha} + \mu^{\alpha})I \\ {}^{C}D^{\alpha}_{0+}R &= A^{\alpha}\rho + \gamma^{\alpha} I - \mu^{\alpha} R, \end{cases} \tag{1} $$

with the initial conditions $S(0) = S_0$, $E(0) = E_0$, $I(0) = I_0$, $R(0) = R_0$, with $S_0, E_0, I_0, R_0 \in \mathbb{R}^{+}_{0}$. The variables S, E, I, R represent the number of susceptible, exposed, infected, and removed, respectively, at time t. The total population is denoted by N. Thus, ${}^{C}D^{\alpha}_{0+}N = A^{\alpha} - \mu^{\alpha} N$, and so the size of the population is not constant in time.

The present paper is organized as follows: Section 2 investigates the existence and uniqueness for the solution of the fractional measles model accompanying the discussion over feasible region, well-posedness, basic reproduction number $(\mathcal{R}_0)$ and stability of the equilibria. It also shows the extent to which $(\mathcal{R}_0)$ is sensitive to each parameter of the model. In Section 3, the measles model is numerically simulated while considering constant transmission rate for monotonically increasing and decreasing infection cases along-with the detailed discussion for the choice of parameters and their estimation through nonlinear least squares technique. Finally, Section 4 concludes the major findings of the present research analysis.

2. Analysis of the Model

Consider the set

$$ \Omega = \{(S, E, I, R) \in (R^{+}_{0})^4 : N \leq A^{\alpha}/\mu^{\alpha}\}. $$

Theorem 1. *With respect to system* (1)*:*

1. *There exists a unique solution to system* (1)*, and the solution is nonnegative.*

2. *The set Ω is invariant with respect to system (1).*
3. $\lim_{t\to\infty} N(t) = A^\alpha/\mu^\alpha$.
4. *For all $t > 0$, $I(t) \leq I_0 + \sigma^\alpha \|E\|_\infty/(\gamma^\alpha + \mu^\alpha)$.*

Proof. The existence and uniqueness of solution for system (1) are a consequence of Theorem 3.1 in [14] (also [14], Remark 3.2). The nonnegativity follows from the fact that

$$ {}^{C}D^{\alpha}_{0+}S|_{S=0},\ {}^{C}D^{\alpha}_{0+}E|_{E=0},\ {}^{C}D^{\alpha}_{0+}I|_{I=0},\ {}^{C}D^{\alpha}_{0+}R|_{R=0} $$

are all nonnegative, and using similar arguments as the ones used in Theorem 2 of [15]. To prove item 2, since ${}^{C}D^{\alpha}_{0+}N = A^\alpha - \mu^\alpha N$, by Theorem 7.2 (and Remark 7.1) of [16], the population size is given by

$$ N(t) = N_0 E_\alpha(-\mu^\alpha t^\alpha) + \int_0^t A^\alpha \tau^{\alpha-1} E_{\alpha,\alpha}(-\mu^\alpha \tau^\alpha) d\tau, $$

where N_0 is the initial population number. With some computations, we arrive at

$$ \begin{aligned} N(t) &= N_0 E_\alpha(-\mu^\alpha t^\alpha) + \int_0^t A^\alpha \tau^{\alpha-1} \sum_{k=0}^{\infty} \frac{(-1)^k \mu^{k\alpha} \tau^{k\alpha}}{\Gamma(k\alpha+\alpha)} d\tau \\ &= \frac{A^\alpha}{\mu^\alpha} + E_\alpha(-\mu^\alpha t^\alpha)\left(N_0 - \frac{A^\alpha}{\mu^\alpha}\right). \end{aligned} \tag{2} $$

Thus, if $N_0 \leq A^\alpha/\mu^\alpha$, then for all $t > 0$, $N(t) \leq A^\alpha/\mu^\alpha$ and we prove that Ω is invariant with respect to system (1). Also, from the relation given in (2), item 3 is immediate. Finally, to prove item 4, from the third equation of (1) and again ([16], Theorem 3.2), we conclude that

$$ I(t) = I_0 E_\alpha(-(\gamma^\alpha + \mu^\alpha)t^\alpha) + \int_0^t \sigma^\alpha E(t-\tau)\tau^{\alpha-1} E_{\alpha,\alpha}(-(\gamma^\alpha + \mu^\alpha)\tau^\alpha) d\tau. $$

Using the relation $E_\alpha(-(\gamma^\alpha + \mu^\alpha)t^\alpha) \leq 1$, we arrive at

$$ \begin{aligned} I(t) &\leq I_0 + \sigma^\alpha \|E\|_\infty \int_0^t \tau^{\alpha-1} E_{\alpha,\alpha}(-(\gamma^\alpha + \mu^\alpha)\tau^\alpha) d\tau \\ &= I_0 + \frac{\sigma^\alpha \|E\|_\infty}{\gamma^\alpha + \mu^\alpha}(1 - E_\alpha(-(\gamma^\alpha + \mu^\alpha)t^\alpha)) \leq I_0 + \frac{\sigma^\alpha \|E\|_\infty}{\gamma^\alpha + \mu^\alpha}. \end{aligned} $$

□

The basic reproduction number of the infection is given by the quotient

$$ R_0 = \frac{A^\alpha \beta^\alpha \sigma^\alpha (1-\rho)}{\mu^\alpha(\sigma^\alpha + \mu^\alpha)(\gamma^\alpha + \mu^\alpha)}, $$

and its value plays an important role to predict the stability of the system.

Theorem 2. *The point $P_F = (A^\alpha/\mu^\alpha(1-\rho), 0, 0, A^\alpha/\mu^\alpha\rho)$ is an equilibrium point of system (1). Also, P_F is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. It is obvious that P_F is an equilibrium point of system (1). The Jacobian matrix of system (1), evaluated at P_F, is

$$ J(P_F) = \begin{bmatrix} -\mu^\alpha & 0 & -\beta^\alpha A^\alpha/\mu^\alpha(1-\rho) & 0 \\ 0 & -\sigma^\alpha - \mu^\alpha & \beta^\alpha A^\alpha/\mu^\alpha(1-\rho) & 0 \\ 0 & \sigma^\alpha & -\gamma^\alpha - \mu^\alpha & 0 \\ 0 & 0 & \gamma^\alpha & -\mu^\alpha \end{bmatrix}, \tag{3} $$

and the spectrum of matrix (3) is

$$\left\{-\mu^{\alpha}, \frac{-(B+C) \pm \sqrt{(B-C)^2+4D}}{2}\right\},$$

where $B = \sigma^{\alpha} + \mu^{\alpha}$, $C = \gamma^{\alpha} + \mu^{\alpha}$, and $D = A^{\alpha}\beta^{\alpha}\sigma^{\alpha}/\mu^{\alpha}(1-\rho)$. Therefore, the eigenvalues are reals and negative if $D < BC$, that is, $R_0 < 1$. In such case, the equilibrium point is locally asymptotically stable [17]. If $R_0 > 1$, then one of the eigenvalues is positive and thus the equilibrium point is unstable. □

One important issue is the sensitivity analysis of the basic reproduction number. Since in many situations we only know an estimation of the parameters, it is important to understand how these approximations influence the value of R_0. The normalized forward sensitivity index of the basic reproduction number R_0, with respect to a given parameter p, is given by [18] $\frac{\partial R_0}{\partial p} \times \frac{p}{R_0}$. The values of the parameters are fixed as (see Section 3 for an explanation) $A = 374125$, $\mu = 0.000525$, $\rho = 0.8$, $\sigma = 2$, and $\gamma = 1.579$. Also, we consider $\alpha = 0.5$ and two values for β: $\beta = 10^{-10}$ and $\beta = 10^{-20}$. The obtained results are displayed in Tables 2 and 3.

Table 2. Sensitivity analysis of $\mathcal{R}_0$: $\beta = 10^{-10}$.

Parameter	Sensitivity Indices
α	-1.411652563
β	$+0.5$
A	$+0.5$
μ	-0.5169256402
ρ	-4
σ	$+0.007971768371$
γ	-0.4910461282

Table 3. Sensitivity analysis of $\mathcal{R}_0$: $\beta = 10^{-20}$.

Parameter	Sensitivity Indices
α	-12.92457802
β	$+0.5$
A	$+0.5$
μ	-0.5169256402
ρ	-4
σ	$+0.007971768371$
γ	-0.4910461282

The parameter with the greatest influence on the value of $\mathcal{R}_0$, when $\beta = 10^{-10}$, is the percentage of vaccination ρ. Hence, it is very important to choose this value when we are modeling the dynamics of the disease. Also, the fractional order α plays an important role in this study. However, when $\beta = 10^{-20}$, it is the fractional order that has most influence on the value of the basic reproduction number.

3. Numerical Simulations

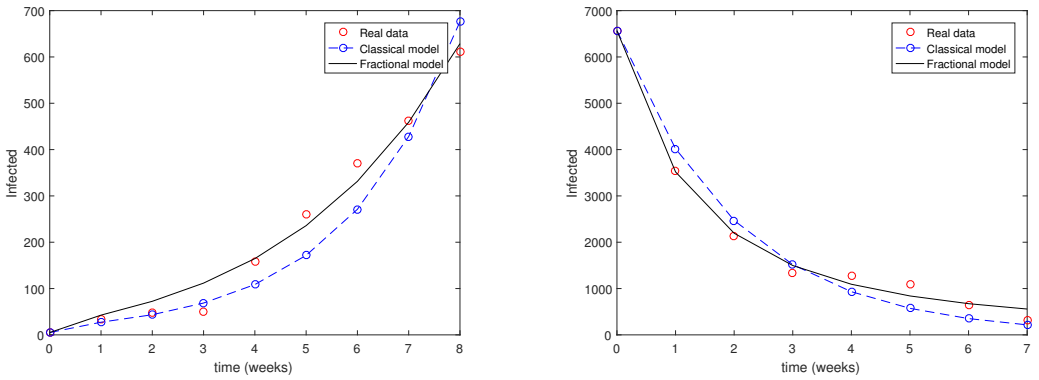
In this section, numerical simulations for both classical and fractional Caputo type model for the measles epidemic proposed in this paper are carried out wherein classical model is simulated under MATLAB ODE solver "*ode45*" and the fractional model under MATLAB FDE solver "*fde12*" [19]. Two cases are separately dealt with. In the first, the transmission rate β is estimated via nonlinear least squares technique while taking the real data from September 2010–May 2011 in monotonically increasing fashion. On the other hand, the second case estimates the transmission rate β while taking the real data from May–December 2018 in monotonically decreasing fashion.

In addition to this, health census in Pakistan estimates that around 80% of the population is vaccinated against measles [20], so $\rho = 0.8$. The birth and death rates are 21.9 births/1000 population and 6.3 deaths/1000 population for 2017 [21]. So, with a population around 205 millions individuals, we fix A = 374,125 month^{-1} and $\mu = 0.000525\,\text{month}^{-1}$. For the rates at which an exposed person becomes infective and when an infected recovers from the disease, we consider the ones given in [11]: $\sigma = 2\,\text{month}^{-1}$ and $\gamma = 1.579\,\text{month}^{-1}$. Remaining parameters for the measles model with increasing and decreasing infection cases are estimated via nonlinear least squares curve fitting technique and listed in the Table 4 along with the residual norms (E) which are smaller for the fractional Caputo type measles model.

Table 4. Best fitted values of the parameters and corresponding residual errors.

Monotonicity	Classical	Fractional
Increasing	$\beta = 1.220959 \times 10^{-8}$ $\alpha = 1.0000$ $E = 1.619008 \times 10^{2}$	$\beta = 1.428694 \times 10^{-22}$ $\alpha = 3.557048 \times 10^{-1}$ $E = 8.407327 \times 10^{1}$
Decreasing	$\beta = 4.0415 \times 10^{-9}$ $\alpha = 1.0000$ $E = 9.1481 \times 10^{2}$	$\beta = 4.5623 \times 10^{-11}$ $\alpha = 8.3680 \times 10^{-1}$ $E = 4.3283 \times 10^{2}$

It can be observed from the Figure 1 that the best fitted curve is obtained via numerical simulations for the fractional versions of the measles model whether the real monthly data follow increasing or decreasing pattern.



(**a**) (**b**)

Figure 1. Profile of infected population from both classical and fractional measles model for the real monthly data with monotonically increasing (**a**) and decreasing (**b**) fashion.

4. Conclusions

A number of mathematical models related with epidemics of different kinds are being proposed to provide health organizations to decide effective strategies to control, eliminate and ultimately eradicate the infectious diseases. However, most of the models are based upon the tools of integer order differentiation and integration which are found to be unuseful in capturing the dynamics of a disease that has non-Markovian characteristics. In this regard, new models with non-local operators possessing memory effects are suggested in the literature.

In this present research work, an epidemiological model of measles epidemic has been fractionalized under the Caputo type non-local operator and compared with its existing classical version with the help of real data application. It has been found that the fractional versions, in cases where the real data set is either monotonically increasing or decreasing, are better than its classical version. This conclusion is based upon the residual error values obtained through nonlinear least

squares curve fitting technique. Furthermore, the fractional Caputo measles model does have a unique solution and its solutions lie the positively invariant region thereby making the model well-posed. Stability analysis showed that the equilibrium point of the fractional model is locally asymptotically stable when its basic reproduction number is less than unity otherwise unstable.

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