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Article

Integer versus Fractional Order SEIR Deterministic and Stochastic Models of Measles

Md Rafiul Islam [1,*], Angela Peace [1], Daniel Medina [2] and Tamer Oraby [2]

[1] Department of Mathematics and Statistics,Texas Tech University, 2500 Broadway, Lubbock, Texas 79409; rafiul.islam@ttu.edu (MR.I.); a.peace@ttu.edu (A.P.)

[2] School of Mathematical and Statistical Sciences, The University of Texas Rio Grande Valley, 1201 W. University Drive, Edinburg, Texas 78539; daniel.medina@utrgv.edu (D.M.); tamer.oraby@utrgv.edu (T.O.)

* Correspondence: rafiul.islam@ttu.edu

Abstract: In this paper, we compare the performance between systems of ordinary and (Caputo) fractional differential equations depicting the susceptible-exposed-infectious-recovered (SEIR) models of diseases. In order to understand the origins of both approaches as mean-field approximations of integer and fractional stochastic processes, we introduce the fractional differential equations as approximations of some type of fractional nonlinear birth–death processes. Then, we examine validity of the two approaches against empirical courses of epidemics; we fit both of them to case counts of three measles epidemics that occurred during the pre-vaccination era in three different locations. While FDEs appear more flexible in fitting empirical data, our ODEs offered better fits to two out of three data sets. Important differences in transient dynamics between these modeling approaches are discussed.

Keywords: fractional SEIR stochastic model; Caputo fractional order differential equations; Measles; Parameter Estimation

1. Introduction

Modeling the spread of infectious diseases before the introduction of vaccines, as well as the validation of these models, has been widely studied since the works of Bernoulli [1], Ross [2], Brownlee [3], Greenwood and Yule [4], Kermack and McKendrick [5], Soper [6], Greenwood [7,8], M . S . Bartlett [9], Bailey [10]. See also Bailey [11] and Anderson [12] for more details about the history of disease modeling. Deterministic models using ordinary differential equations (ODEs) have received great attention [12–16] and wide assimilation by health sciences. See Temime *et al.* [17] and the references therein. Other deterministic models such as difference equations are also used to model the spread of diseases; for instance, see Fisman *et al.* [18]. However, fractional differential equations (FDEs) have been used in the last decade to model the course of epidemics [19–24].

Fractional differential equations are usually used to involve the memory of the process in the dynamics of the systems. There is more than one type of fractional order derivative; most notably, Caputo, Grünwald-Letnikov, and Riemann-Liouville [25]. Here, we study the Caputo fractional order derivative. Integer order derivatives of ordinary differential equations are special cases of fractional order derivatives. It was noted in more than one paper, e.g. [26], that FDEs give a better depiction of the courses of epidemics and natural phenomena than ODEs. Few researchers have fitted their FDE models to data [26,27], however, they lack details on justifying the goodness of fit so as to statistically validate them. This motivated us to compare systems of ODEs and FDEs by fitting them to some actual epidemic data.

Measles is a marker disease for virological, epidemiological, clinical, statistical, geographical, mathematical, and humanitarian reasons [28, p.16-21]. Mathematical modeling of measles epidemics

dates as far as 1888 by D'Enko and then by Hamer [28, p.19]. Regularity and a large number of cases of measles' epidemics with major peaks in the pre-vaccination era (before 1964) support the choice of testing models against measles data. Many other researchers formulated measles models and fit them to data, as in Bjørnstad *et al.* [29], where a time scale of two weeks is recommended fitting the number of cases, and in Yingcun Xia *et al.* [30], where a model is used to examine a spatial network. In this paper, we choose to use data of measles infections in the US and UK in two decades of the pre-vaccination era (1944 − 1964), to compare the goodness of fit of ODEs and FDEs to those epidemics.

While ordinary differential equations are well-established as deterministic models of the spread of diseases (see e.g. Greenwood and Gordillo [31] and Vasilyeva *et al.* [32]), FDE models are sometimes used. However, often these approaches lack mathematical basis or physical interpretation except for exchanging integer differentiation with fractional ones, (see e.g. Almeida *et al.* [26] and Aranda *et al.* [33]). Angstmann *et al.* [34] and Sardar *et al.* [35] provided a valid variation by considering the memory of the non-Markovian infection process. The result is a mixed system of integer and fractional derivatives of the Riemann-Liouville type. Saeedian *et al.* [36] showed how another memory functional of the process can lead to replacing the integer derivatives with Caputo fractional derivatives. In this paper, we show how Caputo fractional differential equations follow naturally from fractional stochastic processes like those introduced in [37–46]. Then we show that for different data sets, FDE models fit the data better for some epidemics whereas ODE models fit better for others. The Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) are used to compare between the fittings of the two models to three data sets. For completeness, we will cover all the required background and the relevant definitions in section 2. That includes a synopsis of Caputo's fractional calculus and fractional stochastic SEIR processes. Section 2 will also include the derivation of the fractional order differential equation depicting the SEIR model from the fractional stochastic SEIR process. It will be followed by the stability analysis of the equilibria of the system of fractional differential equations, which will be then fitted to measles data fitting and simulated.

2. Methods

In this section we provide a background for fractional differentiation and a fractional birth-death process. We also introduce the integer and fractional differential equations for the SEIR model and analyze the stability of the FDE's equilibria.

2.1. Preliminaries

2.1.1. Fractional Calculus

Let D^n be the Leibniz integer-order differential operator given by

$$D^n f = \frac{d^n f}{dt^n} = f^{(n)},$$

and let J^n be an integration operator of integer order given by

$$J^n f(t) = \frac{1}{n!}\int_0^t (t-\tau)^{n-1} f(\tau) d\tau, \tag{1}$$

where $n \in \mathbb{Z}^+$. Let us use $D = D^1$ for the first derivative. We will use $\partial_x^\alpha F := \frac{\partial^\alpha F}{\partial x^\alpha}$ and use $\partial_x F := \frac{\partial F}{\partial x}$.

For fraction-order integrals, we use

$$J^{n-\alpha} f(t) = \frac{1}{\Gamma(n-\alpha)}\int_0^t (t-\tau)^{n-\alpha-1} f(\tau) d\tau, \tag{2}$$

where $n-1 < \alpha \leq n$. Now, define the Caputo fractional differential operator D_*^α to be,

$$D_*^\alpha f(t) = J^{n-\alpha} D^n f(t),$$

where $n-1 < \alpha \leq n$, for $n \in \mathbb{N}$. It is also known that

$$\begin{aligned} \lim_{\alpha \to n} D_*^\alpha f(t) &= f^{(n)}(t), \\ \lim_{\alpha \to n-1} D_*^\alpha f(t) &= f^{(n-1)}(t) - f^{(n-1)}(0) \end{aligned} \tag{3}$$

for any $n \in \mathbb{N}$. We will consider $n = 1$ in this work; that is $0 < \alpha \leq 1$. In that case,

$$J^{1-\alpha} f(t) = \int_0^t f(\tau) dg_t(\tau), \tag{4}$$

where $g_t(\tau) = \frac{1}{\Gamma(2-\alpha)} \left(t^{1-\alpha} - (t-\tau)^{1-\alpha}\right)$. That is for each t, the integral $J^{1-\alpha} f(t)$ is an area under $f(\tau)$, while above $g_t(\tau)$ which works as a deformed or slowed time-scale as illustrated by Podlubny [47].

The generalized mean-value theorem for the Caputo fractional derivative is given as

$$f(x) = f(a) + \frac{1}{\Gamma(\alpha)} D_*^\alpha f(c)(x-a)^\alpha \quad \text{for some} \quad a \leq c \leq x$$

and for all $x \in (a, b]$ whenever $f, D_*^\alpha f \in C([a, b])$, see e.g. Özalp and Demirci [48] .

The Mittag-Leffler is a function that generalizes the exponential function. That function can be written as follows,

$$E_\alpha(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(\alpha k + 1)}, \quad \alpha \in \mathbb{R}^+, \quad z \in \mathbb{C}, \tag{5}$$

or, more generally using two parameters,

$$E_{\alpha,\beta}(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(\alpha k + \beta)}, \quad \alpha, \beta \in \mathbb{R}^+, \quad z \in \mathbb{C}. \tag{6}$$

The general Mittag-Leffler has the following important property for any $\alpha, \beta > 0$

$$E_{\alpha,\beta}(z) = z E_{\alpha,\alpha+\beta}(z) + \frac{1}{\Gamma(\beta)}. \tag{7}$$

Two important differential properties of the Mittag - Leffler function is that

$$D_*^\alpha e^{\lambda t} = t^{-\alpha} E_{1,1-\alpha}(\lambda t) \tag{8}$$

and

$$D_*^\alpha E_{\alpha,1}(\lambda t^\alpha) = \lambda E_{\alpha,1}(\lambda t^\alpha) \tag{9}$$

for any $\lambda > 0$.

2.2. Fractional Stochastic Process

Fix $0 < \alpha \leq 1$. Following Earn *et al.* [49], we consider a compartmental susceptible-exposed-infected-recovered (SEIR) model to depict the measles transmission dynamics in a closed population. Let $X_1^{(\alpha)}$, $X_2^{(\alpha)}$, $X_3^{(\alpha)}$, and $X_4^{(\alpha)}$ be the number of susceptible, exposed, infected, and recovered individuals, respectively, such that $X_1^{(\alpha)} + X_2^{(\alpha)} + X_3^{(\alpha)} + X_4^{(\alpha)} = N$, the population size. Figure 1 shows how the disease is progressing from one sub-population to another.

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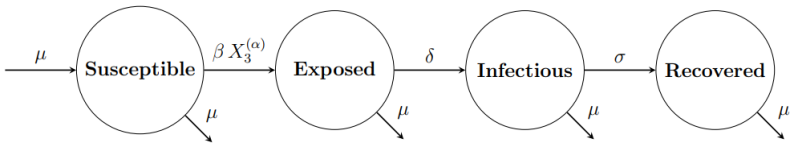

Figure 1. Schematic diagram of the SEIR model depicting transitions between different compartments.

Here, μ is the recruitment and per capita death rate, β is the transmission rate, δ is the rate at which exposed individuals become infectious, and σ is the recovery rate.

A stochastic SEIR model can be depicted using a continuous time Markov chain (CTMC) like the birth and death process with non-linear rates of transition as those given in table 1, see [50, p.22] and [51, p.321]. M . S . Bartlett [9] and Greenwood and Gordillo [31] introduced (integer) stochastic SIR model using CTMC with rates similar to those in the first six rows in table 1 to show a deterministic SIR model of the ODE type depicting the approximate dynamics of the means of the processes. Here, we introduce a fractional SEIR model using a CTMC of fractional birth and death process on triplets (i, j, k) with rates provided by table 1.

Table 1. Transitions and their rates for a birth and death process depicting a stochastic SEIR model.

Transition	Rate
$X_1^{(\alpha)} \to X_1^{(\alpha)} + 1$	μN
$X_1^{(\alpha)} \to X_1^{(\alpha)} - 1$	$\beta X_1^{(\alpha)} \frac{X_3^{(\alpha)}}{N} + \mu X_1^{(\alpha)}$
$X_2^{(\alpha)} \to X_2^{(\alpha)} + 1$	$\beta X_1^{(\alpha)} \frac{X_3^{(\alpha)}}{N}$
$X_2^{(\alpha)} \to X_2^{(\alpha)} - 1$	$(\mu + \delta) X_2^{(\alpha)}$
$X_3^{(\alpha)} \to X_3^{(\alpha)} + 1$	$\delta X_2^{(\alpha)}$
$X_3^{(\alpha)} \to X_3^{(\alpha)} - 1$	$(\mu + \sigma) X_3^{(\alpha)}$
$X_4^{(\alpha)} \to X_4^{(\alpha)} + 1$	$\sigma X_3^{(\alpha)}$
$X_4^{(\alpha)} \to X_4^{(\alpha)} - 1$	$\mu X_4^{(\alpha)}$

An α-fractional SEIR stochastic process $\{(X_1^{(\alpha)}(t), X_2^{(\alpha)}(t), X_3^{(\alpha)}(t)) : t \geq 0\}$ for $0 < \alpha \leq 1$ with state probabilities

$$p_{(i,j,k)}^{(\alpha)}(t) = P((X_1^{(\alpha)}(t), X_2^{(\alpha)}(t), X_3^{(\alpha)}(t)) = (i, j, k) | (X_1^{(\alpha)}(0), X_2^{(\alpha)}(0), X_3^{(\alpha)}(0)) = (i_0, j_0, k_0)$$

for $i, j, k = 0, 1, \ldots$, such that $0 \leq i + j + k \leq N$ and $P((X_1^{(\alpha)}(0), X_2^{(\alpha)}(0), X_3^{(\alpha)}(0)) = (i_0, j_0, k_0)) = 1$, has a fractional forward Kolmogorov equation of the stochastic SEIR model similar to equation (A1) and is given by

$$\begin{aligned} D_*^{\alpha} p_{(i,j,k)}^{(\alpha)}(t) \quad = \quad & \mu N p_{(i-1,j,k)}^{(\alpha)}(t) + \beta(i+1)\frac{k}{N} p_{(i+1,j-1,k)}^{(\alpha)}(t) + \mu(i+1) p_{(i+1,j,k)}^{(\alpha)}(t) \\ & + \delta(j+1) p_{(i,j+1,k-1)}^{(\alpha)}(t) + \mu(j+1) p_{(i,j+1,k)}^{(\alpha)}(t) + (\sigma+\mu)(k+1) p_{(i,j,k+1)}^{(\alpha)}(t) \\ & - (\mu N + \beta i \frac{k}{N} + \mu i + (\delta+\mu) j + (\sigma+\mu) k) p_{(i,j,k)}^{(\alpha)}(t) \end{aligned} \tag{10}$$

with $p_{(i,j,k)}^{(\alpha)}(t) = 0$ if either i, j, or k are negative or more than N. See also Di Crescenzo *et al.* [45]. The classical forward Kolmogorov equation of the stochastic SEIR model follows when $\alpha = 1$ with state probabilities $p_{(i,j,k)}^{(1)}(t)$, [51, p.321]. Equation (10) can be used to find the probability generating

function $G^{(\alpha)}(u,v,w,t) = E(u^{X_1^{(\alpha)}(t)}v^{X_2^{(\alpha)}(t)}w^{X_3^{(\alpha)}(t)})$ of the state probabilities, as the solution of the Cauchy problem

$$\begin{aligned} D_*^\alpha G^{(\alpha)} &= \mu N(u-1)G^{(\alpha)} + \mu(1-u)\partial_u G^{(\alpha)} + (\delta w + \mu - (\delta+\mu)v)\partial_v G^{(\alpha)} \\ &\quad + (\sigma+\mu)(1-w)\partial_w G^{(\alpha)} + \beta\frac{w}{N}(v-u)\partial_{uw}G^{(\alpha)} \end{aligned} \tag{11}$$

for $t > 0$ and $G^{(\alpha)}(u,v,w,0) = u^{i_0}v^{j_0}w^{k_0}$, for $-1 < u,v,w < 1$.

Note that, the integer or classical stochastic SEIR process is $(X_1^{(1)}(t), X_2^{(1)}(t), X_3^{(1)}(t))$ which is simply the case when $\alpha = 1$. But that leads to another interesting fact that defines the relationship between the fractional and integer stochastic SEIR model; that is, the former process is a random-time subordination of the latter one, as established for other fractional processes like the fractional Poisson process [37,45,52], and the fractional birth and/or death processes [39,40,42,43,53].

Theorem 1. *The fractional stochastic SEIR process* $(X_1^{(\alpha)}(t), X_2^{(\alpha)}(t), X_3^{(\alpha)}(t))$ *has the same distribution as the random-time subordinated integer stochastic SEIR process*

$$(X_1^{(1)}(\mathcal{T}_{2\alpha}(t)), X_2^{(1)}(\mathcal{T}_{2\alpha}(t)), X_3^{(1)}(\mathcal{T}_{2\alpha}(t)))$$

for $t > 0$ *and* $0 < \alpha \leq 1$.

The proof is provided in Appendix A.

2.3. Measles' Model via Fractional Differential Equations (FDE)

The means of the three discrete-marginal processes $X_1^{(\alpha)}(t)$, $X_2^{(\alpha)}(t)$, and $X_3^{(\alpha)}(t)$ can be found using $\partial_u G^{(\alpha)}(1,1,1,t)$, $\partial_v G^{(\alpha)}(1,1,1,t)$, and $\partial_w G^{(\alpha)}(1,1,1,t)$, respectively. Let $S^{(\alpha)}(t) := \frac{1}{N}E(X_1^{(\alpha)}(t))$, $E^{(\alpha)}(t) := \frac{1}{N}E(X_2^{(\alpha)}(t))$, and $I^{(\alpha)}(t) := \frac{1}{N}E(X_3^{(\alpha)}(t))$, where N is the total population size and $E(x)$ is the expected value of x. Thus using equation (11), and approximating $E(X_1^{(\alpha)}(t)X_3^{(\alpha)}(t))$ by $E(X_1^{(\alpha)}(t))E(X_3^{(\alpha)}(t))$ we reach the fractional order version of the system of equations that was used by M . S . Bartlett [9] to model measles,

$$\begin{aligned} D_*^\alpha S^{(\alpha)} &= \mu - \beta S^{(\alpha)} I^{(\alpha)} - \mu S^{(\alpha)} \\ D_*^\alpha E^{(\alpha)} &= \beta S^{(\alpha)} I^{(\alpha)} - (\mu+\delta)E^{(\alpha)} \\ D_*^\alpha I^{(\alpha)} &= \delta E^{(\alpha)} - (\mu+\sigma)I^{(\alpha)} \end{aligned} \tag{12}$$

where $S^{(\alpha)}$, $E^{(\alpha)}$, and $I^{(\alpha)}$ be the proportion of susceptible, exposed, and infected individuals, respectively. With proportion of recovered individuals given by $R^{(\alpha)} = 1 - (S^{(\alpha)} + E^{(\alpha)} + I^{(\alpha)})$, we reach the fractional α order SEIR model

$$\begin{aligned} D_*^\alpha S^{(\alpha)} &= \mu - \beta S^{(\alpha)} I^{(\alpha)} - \mu S^{(\alpha)} \\ D_*^\alpha E^{(\alpha)} &= \beta S^{(\alpha)} I^{(\alpha)} - (\mu+\delta)E^{(\alpha)} \\ D_*^\alpha I^{(\alpha)} &= \delta E^{(\alpha)} - (\mu+\sigma)I^{(\alpha)} \\ D_*^\alpha R^{(\alpha)} &= \sigma I^{(\alpha)} - \mu R^{(\alpha)} \end{aligned} \tag{13}$$

with $0 < \alpha \leq 1$. The non-negative parameters β, μ, δ, and σ – denoting them by θ, for brevity – have dimensions given by $\frac{1}{\text{time}^\alpha}$. By construction of the FDE model as a mean field approximation of the α-fractional stochastic SEIR process which in its turn is a subordination of an integer stochastic SEIR process by Theorem 1, those parameters could be interpreted as the rates measured by an independent observer of the process or calculated based on a cosmic time flow [47]. We replace those parameters

with a power α of new parameters; that is, θ_*^α in place of θ so the parameters θ_* will have the dimension of $\frac{1}{time}$ and the system becomes the following form:

$$\begin{aligned} D_*^\alpha S^{(\alpha)} &= \mu_*^\alpha - \beta_*^\alpha S^{(\alpha)} I^{(\alpha)} - \mu_*^\alpha S^{(\alpha)} \\ D_*^\alpha E^{(\alpha)} &= \beta_*^\alpha S^{(\alpha)} I^{(\alpha)} - (\mu_*^\alpha + \delta_*^\alpha) E^{(\alpha)} \\ D_*^\alpha I^{(\alpha)} &= \delta_*^\alpha E^{(\alpha)} - (\mu_*^\alpha + \sigma_*^\alpha) I^{(\alpha)} \\ D_*^\alpha R^{(\alpha)} &= \sigma_*^\alpha I^{(\alpha)} - \mu_*^\alpha R^{(\alpha)} \end{aligned} \tag{14}$$

2.4. Measles' Model via Ordinary Differential Equations (ODE)

The following system of differential equations represents the ordinary differential equation representation of the SEIR model and is the FDE model when $\alpha = 1$ in equation 14.

$$\begin{aligned} DS &= \mu - \beta SI - \mu S \\ DE &= \beta SI - (\mu + \delta) E \\ DI &= \delta E - (\mu + \sigma) I \\ DR &= \sigma I - \mu R \end{aligned} \tag{15}$$

where μ, β, δ, and σ are the model parameters described above. They all have dimensions given by $\frac{1}{\text{time}}$. The last equation in (15) is redundant since $R = 1 - (S + E + I)$.

2.5. Measles' Model via α-dependent Ordinary Differential Equations

We are interest in comparing the FDE vs ODE modeling approaches. It is important to note that the basic ODE case considers $\alpha = 1$, however in the FDE case, α appears in the derivative as well as the parameter values. In order to better compare these two approaches, here we develop an ODE analoge to the FDE that incorporates α in the parameter values. We call this new system the α-dependent ODE. By dropping the α order derivative from the left side and α power from $S^{(\alpha)}$, $E^{(\alpha)}$, and $I^{(\alpha)}$ of equation (14), our α-dependent ODE takes the following form:

$$\begin{aligned} DS &= \mu_*^\alpha - \beta_*^\alpha SI - \mu_*^\alpha S \\ DE &= \beta_*^\alpha SI - (\mu_*^\alpha + \delta_*^\alpha) E \\ DI &= \delta_*^\alpha E - (\mu_*^\alpha + \sigma_*^\alpha) I \\ DR &= \sigma_*^\alpha I - \mu_*^\alpha R \end{aligned} \tag{16}$$

2.6. Model Analysis

Analysis of the ODE is almost the same as of the FDE so we include the FDE one here. We start by proving the positive invariance of the region of solutions of the FDE model. Henceforth, we drop the α from $S^{(\alpha)}$, $E^{(\alpha)}$, and $I^{(\alpha)}$, for brevity.

The following two lemmas of asymptotic behavior of FDEs are given here and their proof in appendix A for completeness.

Lemma 1. *The closed simplex region* $M = \{(S, E, I) \in \mathbb{R}_+^3 : 0 \leq S + E + I \leq 1\}$ *is a positive invariant set for the FDE model in* (14).

We can find the model's equilibrium points by setting $D_*^\alpha S = 0$, $D_*^\alpha E = 0$, and $D_*^\alpha I = 0$. Thus, there are two equilibria to the measles' SEIR model (14). They are:

1. the disease free equilibrium $DFE \equiv (1, 0, 0)$, and

2. the endemic equilibrium

$$EE = (s^*, e^*, i^*) \equiv \left(\frac{1}{R_0}, \frac{\mu}{\delta+\mu}\left(1 - \frac{1}{R_0}\right), \frac{\mu}{\beta}(R_0 - 1) \right).$$

where the basic reproduction number is $R_0 := \frac{\beta\delta}{(\mu+\sigma)(\mu+\delta)}$. EE exists only when $1 < R_0 < 1 + \frac{\beta}{\mu}$.

An equilibrium is locally asymptotically stable if the eigenvalues of the Jacobian matrix of the n-dimensional system, namely $\lambda_1, \lambda_2, \ldots, \lambda_n$, have the property that $|\arg(\lambda_i)| > \frac{\alpha\pi}{2}$, for $i = 1, 2, \ldots, n$, [25, p.158]. Thus, in general, the stability of the ordinary differential equations model implies stability of its fractional counter model. But, here they are equivalent due to the following lemma whose solution could be found in appendix A.

Lemma 2. *The Disease-Free Equilibrium DFE is locally asymptotically stable if* $R_0 < 1$. *The endemic equilibrium EE is is locally asymptotically stable if* $R_0 > 1$.

Therefore, they have the same asymptotic behavior. Yet, the transient behavior differs as will be seen by simulations below.

Moreover, a very important difference is their oscillation behavior is not similar. Let λ_ℓ and u_ℓ for $\ell = 1, 2, \ldots, N$ be the eigenvalues and their respective eigenvectors of an $N \times N$ matrix A. The general solution of initial value problem consisting of a system of N linear fractional differential equations $D^\alpha_* x(t) = Ax(t)$ such that $x(0) = x_0$ can be found to be

$$x(t) = \sum_{\ell=1}^{N} c_\ell u_\ell E_\alpha(\lambda_\ell t^\alpha) \tag{17}$$

for certain constants $c_\ell \in \mathbb{C}$ for $\ell = 1, 2, \ldots, N$ such that $\sum_{\ell=1}^{N} c_\ell u_\ell = x_0$, [25, Theorem 7.13]. In case that $\alpha = 1$, we recover the known solution of the system of ODEs given by

$$x(t) = \sum_{\ell=1}^{N} c_\ell u_\ell \exp(\lambda_\ell t).$$

If $N = 3$ and A is not a symmetric matrix then at least one of the eigenvalues is a real-valued number and the other two eigenvalues , say λ_2 and λ_3, are conjugate complex-valued. In that situation, $x(t)$ would oscillate with inter-peak periods, called inter-epidemic period in disease modeling, given by $2\pi(\Im(\lambda_2))^{-1}$ [14]. If $\Re(\lambda_\ell) < 0$ for all ℓ then the oscillations will be damped to zero. That damped oscillation is clear in the case of $\alpha = 1$ due to the exponential damping in the superposition of the sine and cosine functions. That behavior, however, is not straight forward for $0 < \alpha < 1$.

2.7. Numerical Simulations

Since the mean of the subordinator process is $E(\mathcal{T}_\alpha(t)) = \dfrac{t^\alpha}{\Gamma(\alpha+1)}$, we use a method similar to that was introduced in Demirici and Özalp [54] to find approximate solutions to initial value FDE problems. We use that method here to simulate the solution of the FDE measles SEIR model. Consider the initial value problem

$$\begin{aligned} D^\alpha_* x(t) &= f(t, x(t)), \text{ for } 0 < t \leq T, \\ x(0) &= x_0, \end{aligned} \tag{18}$$

for some $T > 0$. A solution of (18) is approximated by the deterministic time subordination

$$x(t) = y\left(\frac{t^\alpha}{\Gamma(\alpha+1)}\right), \tag{19}$$

of $y(s)$, the solution of the ordinary differential equation

$$\begin{aligned} \frac{dy(s)}{ds} &= g(s, y(s)), \text{ for } 0 < s \leq \frac{t^\alpha}{\Gamma(\alpha+1)} \\ y(0) &= x_0. \end{aligned} \tag{20}$$

where

$$g(s, y(s)) = f(t - (t^\alpha - s\Gamma(\alpha+1))^{\frac{1}{\alpha}}, x(t - (t^\alpha - s\Gamma(\alpha+1))^{\frac{1}{\alpha}})). \tag{21}$$

for all $0 < t \leq T$, [54].

We use the subordination of the solution of ODEs to FDEs represented in equations (19) and (20) to numerically simulate solutions of FDEs, see algorithm 1.

Algorithm 1 Numerical solution of $D_*^\alpha x(t) = f(t, x(t))$ for $0 < t < T$ with $x(0) = x_0$.

Input: $\alpha, T, f(t, x(t)), m, n$ Output: $x(t)$
begin
Divide the interval $[0, T]$ into n sub-intervals using

$$0 = t_0 < t_1 < \ldots < t_n = T.$$

for $i = 1, 2, \ldots, n$
Divide the interval $[0, \frac{t_i^\alpha}{\Gamma(\alpha+1)}]$ into further m sub-intervals using

$$0 = s_0 < s_1 < \ldots < s_m = \frac{t_i^\alpha}{\Gamma(\alpha+1)}.$$

Solve the system $Dy(s) = f(t_i - (t_i^\alpha - s\Gamma(\alpha+1))^{\frac{1}{\alpha}}, y(s))$ with $y(0) = x_0$ using Euler or Runge-Kutta methods on $s_0, s_1, \ldots, s_m$.
Retain $x(t_i) = y(s_m)$.
end
Return $[x_0, x(t_1), x(t_2), \ldots, x(t_n)]$.
end

2.8. Fitting FDE and ODE models to measles data

We use the method of ordinary least squares (OLS) to fit the FDE model to the data by minimizing the objective function

$$L(\alpha, \beta, \mu, \delta, \sigma) = \sum_{i=1}^{n} (I_i^{(d)} - I_i^{(s)})^2$$

for $\alpha \in (0, 1]$, and $\beta, \mu, \delta, \sigma \in (0, \infty)$, where $I^{(d)}$ is the data of actual proportion of infections and $I^{(s)}$ is the simulated proportion of infections. The values $I_i^{(s)}$ approximating $I(t_i)$ are found by solving the FDE model using algorithm 1.

Parameter estimation was conducted using Matlab MultiStart and fmincon functions. MultiStart carries out the optimization procedure using initial points within the parameters' spaces. It generates some initial points depending on a converging algorithm. The fmincon finds a local minimum for the constrained nonlinear multivariable function. The MultiStart together with fimincon do the global optimization of a nonlinear multivariable function. The MultiStart function uses parallel processing which drastically reduces the running time.

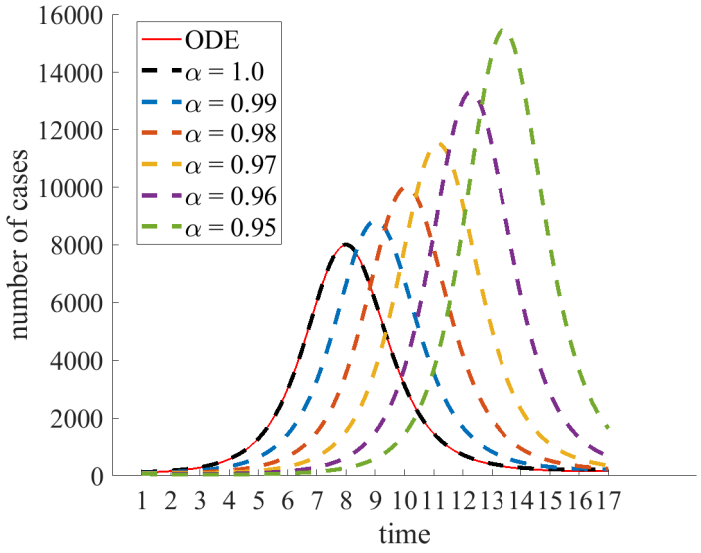

Figure 2. Number of cases using classical ODE model and FDE model with different fractional orders α. The simulations are done using $\mu = \mu_\star = 0.0027$, $\beta = \beta_\star = 119.2257$, $\delta = \delta_\star = 16.7301$, and $\sigma = \sigma_\star = 10.1873$.

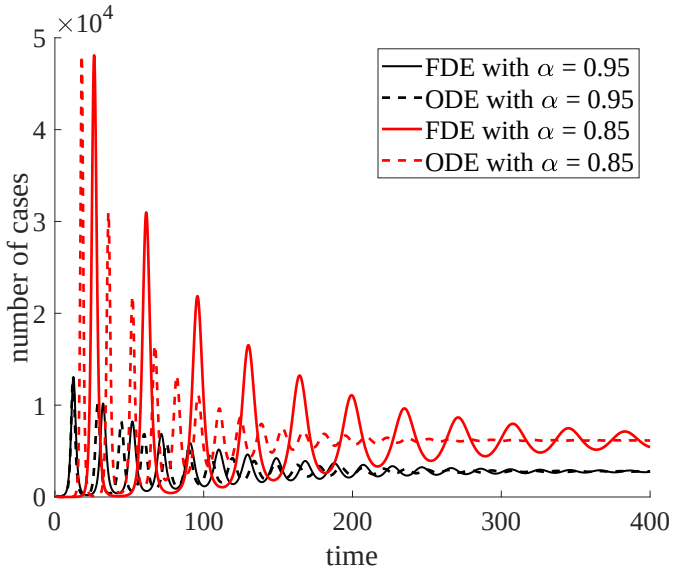

Figure 3. Number of cases using FDEM and its analogous ODEM with different fractional orders α. The simulations are done using $\mu_\star = 0.0027$, $\beta_\star = 119.2257$, $\delta_\star = 16.7301$, and $\sigma_\star = 10.1873$.

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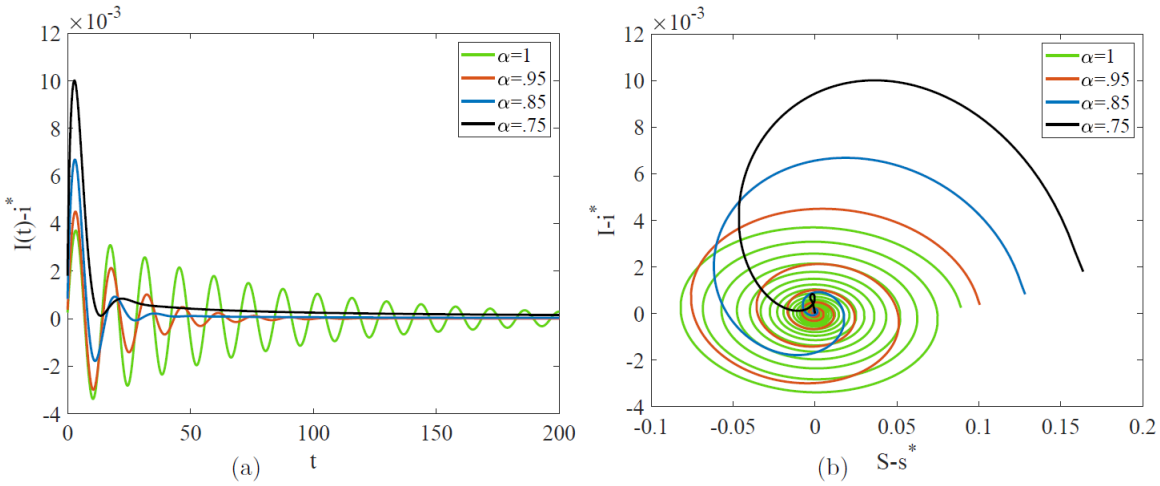

Figure 4. Simulations of solutions of the SEIR FDE centered about the endemic equilibrium (EE) for $\alpha = 1, .95, .85$, and $.75$ using equation (17) shows a suppression of damped oscillations as α decreases. The simulations are done using $\mu_\star = 0.0027, \beta_\star = 119.2257, \delta_\star = 16.7301$, and $\sigma_\star = 10.1873$.

3. Results

We solve the system of FDE (equation 14) using algorithm 1 and the systems of ODE (equations 15 and 16) using the Runge-Kutta method.

Simulations of the classical ODE (equation 15) and FDE (equation 14), Figure 2, shows that the system of fractional differential equations is very sensitive to its order of differentiation α. For smaller α, the peak number of cases of the epidemic is larger but the duration of the outbreak is shorter. The solution of the FDE model converges to the solution of the classical ODE as $\alpha \to 1$. To further compare the two modeling approaches, we consider the analogue ODEs derived for specific α values, see equation (16). These comparisons are shown in Figure 3. During transient dynamics both models exhibit several peaks in the number of cases. The number of these peaks and their respective amplitudes are similar between models, however there are differences in the timing of these peaks. The transient oscillations of the FDE model are more stretched out than its ODE analogue, and its solutions experience longer inter-epidemic times. Both models approach the same equilibria solutions.

Simulations of equation (17) in Figure 4 shows that disease models of fractional order equations lack the same oscillatory behavior exhibited by systems of ODEs with conjugate complex eigenvalues of the Jacobian matrices calculated at endemic equilibrium.

The models were fitted to three measles' epidemics in the pre-vaccination era in three different cities: New York, London, and Portsmouth. Simulations of the fitted ODE and FDE models are shown in Figure 5. See also Appendix B for the data and the parameter estimates. The estimate of α are $0.99, 0.99$, and 0.88 for New York, London, and Portsmouth respectively. The AIC and BIC are found to be smaller for ODE models for the epidemics in New York and London with values of AIC(ODE)= 250.539 and 389.358 and BIC(ODE)= 253.872 and 394.541, respectively, while AIC(FDE)= 255.360 and 413.275 and BIC(FDE)= 259.526 and 419.754, respectively. For Portsmouth's epidemic, the results are the opposite, AIC(ODE)= 277.938 and BIC(ODE)= 282.978 while AIC(FDE)= 271.920 and BIC(FDE)= 278.213. Yet the differences between the fitting of ODE and FDE models are not striking.

4. Discussion

Replacing first order derivatives with Caputo fractional derivatives has been the practice for many studies using fractional order modeling of diseases. In this paper, we show how those models follow from an approximation to the dynamical system governing the means of fractional stochastic SEIR processes. Moreover, we study ordinary and fractional order systems of differential equations of SEIR models using three data sets of measles epidemics in three different cities selected from the

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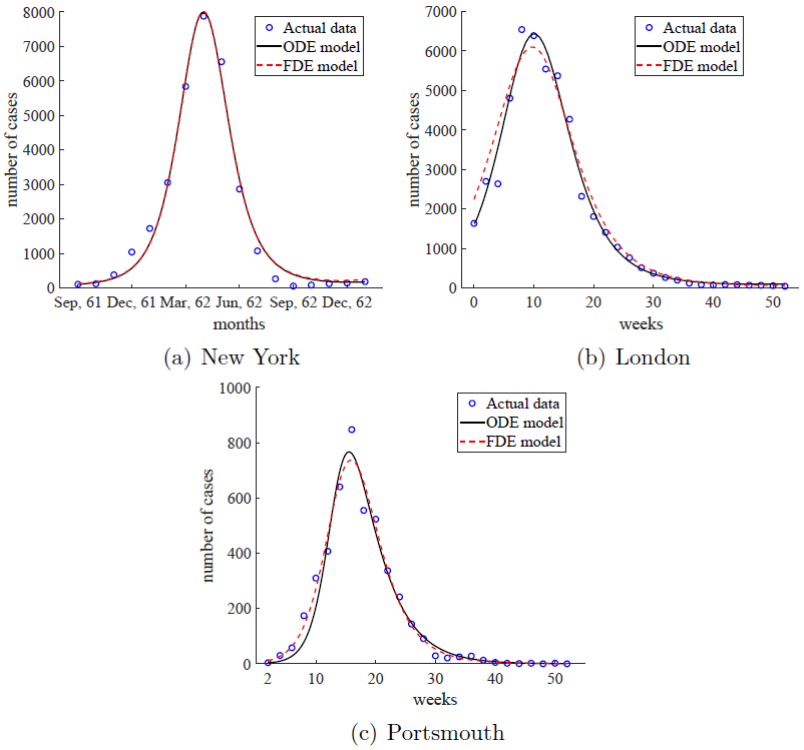

Figure 5. Simulations of ODE and FDE models fitted to measles epidemics in the pre-vaccination era.

pre-vaccination era. It appears that, in some situations, the fractional order differential equation model (FDEM) gives better fit than the ordinary differential equation model (ODEM).

Angstmann *et al.* [34] use the master equation of a continuous-time random walk to derive an FDEM involving Riemann-Liouville fractional derivatives. Power laws are postulated to model time of infectiousness and recovery. That extension from exponential times in ordinary differential equations is a different approach from the mean field approximation of a stochastic process. Saeedian *et al.* [36] introduced the Caputo fractional differential equations through a memory of the whole process of infection and disease recovery. In our paper, we have considered, for the first time, fractional stochastic SEIR model and have shown how the Caputo fractional differential equations follows as mean-field approximation of the process.

Fractional stochastic SEIR model introduced here turns out to be a random-time subordination of a classical stochastic SEIR model. Other real-life systems are modeled using a subordination of a stochastic process. A subordinated process was introduced by Mandelbrot and Taylor [55] to model the logarithm of market prices where the original process is a Brownian motion subordinated by a stochastic time process $\mathcal{T}_{2\alpha}$, which is the same random time process we have found here. In Mandelbrot and Taylor [55], the stochastic time process $\mathcal{T}_{2\alpha}$ is called the operational time and t is the physical time.

Further study of the fractional stochastic SEIR model might lead to interesting dynamical behaviors. For instance, it can provide more insights into the stochastic oscillations of the disease in a more flexible way than their classical counterparts. Thus, studying the fractional stochastic SEIR model is the next step in this work.

5. Conclusion

In this paper, we compare two deterministic models of disease: ordinary differential equations (ODE) and fractional differential equations (FDE). We use three different data sets of measles epidemics from the pre-vaccination era. We also explain FDEs as the mean-field approximation of a fractional

stochastic SEIR model. Up to our knowledge, this is the first time such a fractional stochastic process is introduced and connected to the fractional order differential equations.

While ODE models are regularly used to model epidemics, such as measles, FDEs seem to have the potential to offer improved model fitting. Rates of transition between compartments in that case could be interpreted as rates with respect to an external observer with a different type of clock, may be due to delay in reporting.

Author Contributions: Conceptualization, MR.I., A.P. and T.O.; methodology, MR.I., D.M. and T.O.; software, MR.I. and T.O.; validation, MR.I. and T.O.; formal analysis, MR.I. and T.O..; investigation, MR.I. and T.O.; data curation,MR.I. and T.O.; writing–original draft preparation, MR.I., D.M.,A.P. and T.O.; writing–review and editing, MR.I., A.P. and T.O.; visualization, MR.I., A.P., D.M. and T.O.; supervision, A.P. and T.O.; funding acquisition, A.P.

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Appendix A. Some Definitions and Proofs

Laplace transform of a function $f(t)$ is defined as

$$\mathcal{L}(f)(s) = \hat{f}(s) = \int_0^\infty e^{-st} f(t) dt.$$

The inverse transform is defined by

$$\mathcal{L}^{-1}(\hat{f})(t) = \frac{1}{2\pi i} \int_{\mathcal{C}} e^{st} \hat{f}(s) ds$$

where $\mathcal{C}$ is a contour parallel to the imaginary axis and to the right of the singularities of $\hat{f}$. The Laplace transform of the Caputo fractional derivative is given by

$$\mathcal{L}(D_*^\alpha f)(s) = s^\alpha \hat{f}(s) - s^{\alpha-1} f(0).$$

Fractional Birth and Death Process:

An α-fractional nonlinear birth and death process $\{N_\alpha(t) : t \geq 0\}$ for $0 < \alpha \leq 1$ with state probabilities

$$p_n^\alpha(t) = P(N_\alpha(t) = n | N_\alpha(0) = 1)$$

for $n \geq 0$ is defined through the forward Kolmogorov (difference-)differential equations

$$D_*^\alpha p_n^\alpha(t) = \lambda_{n-1} p_{n-1}^\alpha(t) + \mu_{n+1} p_{n+1}^\alpha(t) - (\lambda_n + \mu_n) p_n^\alpha(t) \tag{A1}$$

for $n \geq 0$ [39,43,53]. The rates λ_n and μ_n are non-negative. The classical birth and death process follows when $\alpha = 1$ with state probabilities $p_n^1(t)$. When $\lambda_n = \lambda$ and $\mu_n = 0$ for all n, the α-fractional nonlinear birth and death process becomes the α-fractional Poisson process [37,41,46]. There, it has shown that $N_\alpha(t)$ has the same probability distribution as $N(\mathcal{T}_\alpha(t))$, where $N(t)$ is the classical birth and death process which is independent of a random time process $\mathcal{T}_\alpha(t)$; that is, a birth and death process subordinated by an α-stable time process.

The random time process $\mathcal{T}_\alpha(t)$ has a distribution given by the folded solution of the fractional diffusion equation $\partial_t^\alpha F = \partial_x^2 F$ for $0 < \alpha \leq 2$, $x \in \mathbb{R}$, $t > 0$, and subject to $F(x,0) = \delta(x)$ for $0 < \alpha \leq 2$ and $\partial_t^\alpha F(x,0) = 0$ for $1 < \alpha \leq 2$, [43]. We will denote its measure by $\nu_{\alpha,t}(ds) := P(\mathcal{T}_\alpha(t) \in ds)$. It has a Laplace transform

$$\mathcal{L}(\nu_{\alpha,s})(r) = \int_0^\infty e^{-rt} \nu_{\alpha,t}(dt) = r^{\frac{\alpha}{2}-1} e^{-sr^{\frac{\alpha}{2}}}$$

and moments $E[(\mathcal{T}_\alpha(t))^k] = \Gamma(k+1)\frac{t^{k\alpha}}{\Gamma(k\alpha+1)}$ for $k = 1, 2, \ldots$; [46,56].

Note that, the absolute values of partial derivatives of G are finite; that is, $|\partial^{(i,j,k)}_{u,v,w} G| < \infty$ for any $i, j, k = 0, 1, 2, \ldots$. That is true since $|u|, |v|, |w| < 1$ and the population size is finite. Thus, switching integrals with derivatives or summations below are valid.

Proof of the Theorem 1

We are going to show that Laplace transform of the probability generating function of the process

$$(X_1^{(1)}(\mathcal{T}_{2\alpha}(t)), X_2^{(1)}(\mathcal{T}_{2\alpha}(t)), X_3^{(1)}(\mathcal{T}_{2\alpha}(t)))$$

is the same as Laplace transform $\hat{G}$ of G, that solves equation (11). From there we will conclude that the two probability distributions are the same since the probability generating function of $(X_1^{(\alpha)}(t), X_2^{(\alpha)}(t), X_3^{(\alpha)}(t))$, by construction, is also a solution to the Cauchy problem in equation (11).

From equation (11), the Laplace transform $\hat{G}$ is the solution of

$$\begin{aligned} s^\alpha \hat{G}^{(\alpha)} - s^{\alpha-1} u^{i_0} v^{j_0} w^{k_0} &= \mu N(u-1)\hat{G}^{(\alpha)} + \mu(1-u)\partial_u \hat{G}^{(\alpha)} + (\delta w + \mu - (\delta+\mu)v)\partial_v \hat{G}^{(\alpha)} \\ &\quad + (\sigma+\mu)(1-w)\partial_w \hat{G}^{(\alpha)} + \beta\frac{w}{N}(v-u)\partial_{uw}\hat{G}^{(\alpha)} \end{aligned} \tag{A2}$$

Let $H^{(\alpha)}(u, v, w, t)$ be the probability generating function of the state probabilities

$$q^{(\alpha)}_{(i,j,k)}(t) = P((X_1^{(1)}(\mathcal{T}_{2\alpha}(t)), X_2^{(1)}(\mathcal{T}_{2\alpha}(t)), X_3^{(1)}(\mathcal{T}_{2\alpha}(t))) = (i, j, k)|$$

$$(X_1^{(1)}(\mathcal{T}_{2\alpha}(0)), X_2^{(1)}(\mathcal{T}_{2\alpha}(0)), X_3^{(1)}(\mathcal{T}_{2\alpha}(0))) = (i_0, j_0, k_0)).$$

That means that

$$\begin{aligned} H^{(\alpha)}(u, v, w, t) &= E(u^{X_1^{(1)}(\mathcal{T}_{2\alpha}(t))} v^{X_2^{(1)}(\mathcal{T}_{2\alpha}(t))} w^{X_3^{(1)}(\mathcal{T}_{2\alpha}(t))}) \\ &= \sum_i \sum_j \sum_k u^i v^j w^k q^{(\alpha)}_{(i,j,k)}(t) \\ &= \sum_i \sum_j \sum_k u^i v^j w^k \int_0^\infty p^{(1)}_{(i,j,k)}(s) \nu_{2\alpha,t}(ds) \\ &= \int_0^\infty (\sum_i \sum_j \sum_k u^i v^j w^k p^{(1)}_{(i,j,k)}(s)) \nu_{2\alpha,t}(ds) \\ &= \int_0^\infty G^{(1)}(u, v, w, s) \nu_{2\alpha,t}(ds). \end{aligned}$$

Thus the Laplace transform of the probability generating function $H^{(\alpha)}$ is given by

$$\begin{aligned} \hat{H}^{(\alpha)}(u, v, w, r) &= \int_0^\infty e^{-rt} \int_0^\infty G^{(1)}(u, v, w, s) \nu_{2\alpha,t}(ds) dt \\ &= r^{\alpha-1} \int_0^\infty G^{(1)}(u, v, w, s) e^{-sr^\alpha} ds \\ &= r^{\alpha-1} \hat{G}^{(1)}(u, v, w, r^\alpha) \end{aligned}$$

Now, the Laplace transform of the probability generating function of the process $(X_1^{(1)}(t), X_2^{(1)}(t), X_3^{(1)}(t))$ also solves (A2) when $\alpha = 1$ which is

$$\begin{aligned} s\hat{G}^{(1)} - u^{i_0}v^{j_0}w^{k_0} &= \mu N(u-1)\hat{G}^{(1)} + \mu(1-u)\partial_u\hat{G}^{(1)} + (\delta w + \mu - (\delta+\mu)v)\partial_v\hat{G}^{(1)} \\ &\quad +(\sigma+\mu)(1-w)\partial_w\hat{G}^{(1)} + \beta\frac{w}{N}(v-u)\partial_{uw}\hat{G}^{(1)}. \end{aligned} \tag{A3}$$

If we substitute with $s = r^\alpha$ in equation (A3) and multiply both sides by $r^{\alpha-1}$ we get

$$\begin{aligned} r^\alpha\hat{H}^{(\alpha)} - r^{\alpha-1}u^{i_0}v^{j_0}w^{k_0} &= \mu N(u-1)\hat{H}^{(\alpha)} + \mu(1-u)\partial_u\hat{H}^{(\alpha)} + (\delta w + \mu - (\delta+\mu)v)\partial_v\hat{H}^{(\alpha)} \\ &\quad +(\sigma+\mu)(1-w)\partial_w\hat{H}^{(\alpha)} + \beta\frac{w}{N}(v-u)\partial_{uw}\hat{H}^{(\alpha)} \end{aligned} \tag{A4}$$

which is the same as equation (A2). This completes the proof.

Proof of Lemma 1

Starting on the S-axis when $E(0) = I(0) = 0$ and $1 \geq S(0) = S_0 \geq 0$, then

$$S(t) = t^\alpha E_{\alpha,\alpha+1}(-\mu t^\alpha)(\mu) + E_{\alpha,1}(-\mu t^\alpha)S_0 \geq 0$$

since $\mu > 0$ and $t \geq 0$. Starting on the E-axis when $S(0), I(0) = 0$ and $E(0) = E_0 \geq 0$, then

$$E(t) = E_{\alpha,1}(-(\mu+\delta)t^\alpha)E_0 \geq 0$$

Starting on the I-axis when $S(0), E(0) = 0$ and $I(0) = I_0 \geq 0$, then

$$I(t) = E_{\alpha,1}(-(\mu+\sigma)t^\alpha)I_0 \geq 0$$

Thus, all axes are positive invariant, for $S(0), E(0), I(0) \geq 0$.

If the solution of the system is leaving through the positive quadrant of the E-I plane, then $S(t_e) = 0$, and $E(t_e)$ and $I(t_e) > 0$ for some $t_e > 0$ such that $S(t) \leq S(t_e)$, for all $t > t_e$. But, $D_*^\alpha S|_{t=t_e} = \mu > 0$. By the generalized mean value theorem

$$S(t) = S(t_e) + \frac{1}{\Gamma(\alpha)}D_*^\alpha S(\tau)(t-t_e)^\alpha$$

for some $t_e \leq \tau < t$, then $S(t) > S(t_e)$ contradicting the original statement. The same argument could be used for the positive quadrant of the S-I plane with $D_*^\alpha E|_{t=t_e} = \beta S(t_e)I(t_e) > 0$ and for the positive quadrant of the E-S plane with $D_*^\alpha I|_{t=t_e} = \alpha E(t_e) > 0$.
To show that $S(t) + E(t) + I(t) \leq 1$ for all $t > 0$, if $S(0) + E(0) + I(0) \leq 1$,

$$\begin{aligned} D_*^\alpha(S+E+I) &= \mu - \mu(S+E+I) - \sigma I \\ &\leq \mu - \mu(S+E+I) \end{aligned} \tag{A5}$$

Thus,

$$\begin{aligned} S(t) + E(t) + I(t) &\leq t^\alpha E_{\alpha,\alpha+1}(-\mu t^\alpha)\mu + E_{\alpha,1}(-\mu t^\alpha)(S(0)+E(0)+I(0)) \\ &\leq t^\alpha E_{\alpha,\alpha+1}(-\mu t^\alpha)\mu + E_{\alpha,1}(-\mu t^\alpha) = 1 \end{aligned} \tag{A6}$$

by equation (7).

Proof of Lemma 2

For the local stability of a disease-free equilibrium, we must evaluate the Jacobian matrix at $DFE \equiv (1,0,0)$

$$J(DFE) = \begin{bmatrix} -\mu & 0 & -\beta \\ 0 & -(\mu+\delta) & \beta \\ 0 & \delta & -(\mu+\sigma) \end{bmatrix}$$

The eigenvalues of the matrix J are,

$$\lambda_1 = -\mu,$$

$$\lambda_2 = \frac{-(\delta+2\mu+\sigma) - \sqrt{\Delta}}{2},$$

$$\lambda_3 = \frac{-(\delta+2\mu+\sigma) + \sqrt{\Delta}}{2},$$

where $\Delta = \delta^2 + 4\delta\beta - 2\delta\sigma + \sigma^2$. From this it is clear that λ_1 is negative and since

$$\Delta = \delta^2 + 4\delta\beta - 2\delta\sigma + \sigma^2 = (\delta-\sigma)^2 + 4\delta\beta > 0$$

then λ_2 and λ_3 are real-valued numbers. Hence $\lambda_2 < 0$. But, $\lambda_3 < 0$ is true when

$$\frac{-(\delta+2\mu+\sigma) + \sqrt{\delta^2 + 4\delta\beta - 2\delta\sigma + \sigma^2}}{2} < 0$$

which is equivalent to $\beta\delta < (\mu+\sigma)(\mu+\delta)$, proving the first part.

The Jacobian matrix calculated at EE is given by

$$J(EE) = \begin{bmatrix} -\mu R_0 & 0 & -\beta\frac{1}{R_0} \\ \mu(R_0-1) & -(\mu+\delta) & \beta\frac{1}{R_0} \\ 0 & \delta & -(\mu+\sigma) \end{bmatrix}$$

which has a characteristic polynomial,

$$-\lambda^3 - \lambda^2[(\mu+\delta)+(\mu+\sigma)+\mu R_0] - \lambda[\mu R_0(2\mu+\delta+\sigma)] + \mu(R_0-1)(\mu+\sigma)(\mu+\delta).$$

Because that polynomial has a degree of 3, we choose to test the Routh-Hurwitz conditions to see if EE is stable.

$$a_1 = \mu R_0 + (2\mu+\delta+\sigma) > 0$$

$$a_3 = \mu(R_0-1)(\mu+\sigma)(\mu+\delta) > 0$$

With these conditions we check that the determinant, $D_2 > 0$.

$$D_2 = a_1 a_2 - a_3 = (\mu R_0 + 2\mu + \delta + \sigma)(\mu R_0(2\mu+\delta+\sigma)) - (\mu(R_0-1)(\mu+\sigma)(\mu+\delta))$$

$$= \mu[\mu R_0^2(2\mu+\delta+\sigma) + (2\mu+\delta+\sigma)^2 R_0 - R_0(\mu+\sigma)(\mu+\delta) + (\mu+\sigma)(\mu+\delta)]$$

$$= \mu[\mu R_0^2(2\mu+\delta+\sigma) + (\mu+\sigma)^2 R_0 + (\mu+\delta)^2 R_0 + (\mu+\sigma)(\mu+\delta)R_0 + (\mu+\sigma)(\mu+\delta)] > 0$$

From this, all Routh-Hurwitz conditions are met and all the eigenvalues of the Jacobian matrix at EE are negative, meaning that $|Re(\lambda_k)| < 0, k = 1,2,3$.

Appendix B. Data Sets and Parameter Estimation

Appendix B.1. New York

Monthly reported infections of measles from September 1961 to January 1963 in New York city are given in table A1. Parameter estimation of Measles New York data from September 1961 to January 1963 using both ODE model and FDE model. The estimated parameters values for the classical ODE model are $(\mu, \beta, \delta, \sigma) = (0.0028, 119.22, 16.73, 10.19)$ with the sum of square error, $SSE = 1.29 \times 10^6$ and for the FDE model are $(\alpha, \mu, \beta, \delta, \sigma) = (0.99, 0.0029, 116.34, 19.39, 10.37)$ with the sum of square error, $SSE = 1.34 \times 10^6$.

Table A1. Reported infections of measles from September 1961 to January 1963 in New York, US.

Year	Months	Cases	Year	Months	Cases	Year	Months	Cases
1961	September	109	1962	March	5839	1962	September	58
1961	October	123	1962	April	7875	1962	October	86
1961	November	383	1962	May	6555	1962	November	125
1961	December	1043	1962	June	2866	1962	December	145
1962	January	1725	1962	July	1075	1963	January	184
1962	February	3056	1962	August	266			

Appendix B.2. London

Biweekly reported infections of measles in 1961 in London, United Kingdom are given in table A2. Parameter estimation of measles Portsmouth data in 1961 using both ODE model and FDE model. The estimated parameters values for the classical ODE model are $(\mu, \beta, \delta, \sigma) = (6.79 \times 10^{-4}, 153.44, 1.99, 4.27)$ with the sum of square error, $SSE = 2.01 \times 10^6$ and for the FDE model are $(\alpha, \mu, \beta, \delta, \sigma) = (0.99, 8.53 \times 10^{-4}, 62.89, 5.37, 4.95)$ with the sum of square error, $SSE = 4.37 \times 10^6$.

Table A2. Biweekly reported measles infections in 1961 in London, UK.

Year	Weeks	Cases	Year	Weeks	Cases	Year	Weeks	Cases	Year	Weeks	Cases
1961	0	1636	1961	14	5374	1961	28	514	1961	42	89
1961	2	2700	1961	16	4272	1961	30	375	1961	44	87
1961	4	2639	1961	18	2322	1961	32	265	1961	46	73
1961	6	4805	1961	20	1810	1961	34	199	1961	48	70
1961	8	6543	1961	22	1409	1961	36	121	1961	50	59
1961	10	6389	1961	24	1037	1961	38	86	1961	52	45
1961	12	5545	1961	26	767	1961	40	76			

Appendix B.3. Portsmouth

Biweekly reported infections of measles in 1961 in Portsmouth, United Kingdom are given in table A3. Parameter estimation of measles Portsmouth data in 1961 using both ODE model and FDE model. The estimated parameters values for the classical ODE model are $(\mu, \beta, \delta, \sigma) = (10^{-6}, 228.61, 0.46, 3.33)$ with the sum of square error, $SSE = 4.57 \times 10^4$ and for the FDE model are $(\alpha, \mu, \beta, \delta, \sigma) = (0.88, 2.56 \times 10^{-4}, 278.72, 1.52, 5.24)$ with the sum of square error, $SSE = 3.22 \times 10^4$.

Table A3. Biweekly reported infections of measles in 1961 in Portsmouth, UK.

weeks	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32
cases	4	30	58	174	310	407	640	847	555	523	337	242	144	91	29	21
weeks	34	36	38	40	42	44	46	48	50	52						
cases	25	28	13	5	2	1	2	0	2	0						

Appendix B.4. Parameter Estimations

Table A4. Comparison between the classical ODE model and FDE model using different data sets

Data	Model	Estimated Parameters, $(\alpha, \mu, \beta, \delta, \sigma)$	SSE
New York	ODE	$(Na, 0.0028, 119.22, 16.73, 10.19)$	1.29×10^6
	FDE	$(0.99, 0.0029, 116.34, 19.39, 10.37)$	1.34×10^6
Portsmouth	ODE	$(Na, 10^{-6}, 228.61, 0.46, 3.33)$	4.57×10^4
	FDE	$(0.88, 2.52 \times 10^{-4}, 278.72, 1.52, 5.24)$	3.22×10^4
London	ODE	$(Na, 6.79 \times 10^{-4}, 153.44, 1.99, 4.27)$	2.01×10^6
	FDE	$(0.99, 8.52 \times 10^{-4}, 62.89, 5.37, 4.95)$	4.36×10^6

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