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A fractional order epidemic model for the simulation of outbreaks of influenza A(H1N1)

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In this paper, we propose a nonlinear fractional order model in order to explain and understand the outbreaks of influenza A(H1N1). In the fractional model, the next state depends not only upon its current state but also upon all of its historical states. Thus, the fractional model is more general than the classical epidemic models. In order to deal with the fractional derivatives of the model, we rely on the Caputo operator and on the Grünwald–Letnikov method to numerically approximate the fractional derivatives. We conclude that the nonlinear fractional order epidemic model is well suited to provide numerical results that agree very well with real data of influenza A(H1N1) at the level population. In addition, the proposed model can provide useful information for the understanding, prediction, and control of the transmission of different epidemics worldwide. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: epidemic models; fractional order model; influenza A(H1N1); Grünwald–Letnikov method

1. Introduction

The pandemic virus AH1N1/09 is a flu virus of swine, avian, and human origin that was first identified in April 2009 in Mexico and the USA [1]. The virus soon spread to the rest of the world and on June 11, 2009; the WHO declared the new influenza A(H1N1) a pandemic [1]. The transmission of the virus AH1N1 is only possible through effective contacts of a susceptible individual with an infectious individual. Typical interventions to control the spread include quarantine, isolation, travel restrictions, closing of public places, fear-based self-quarantine, and cancelation of events [1]. These interventions have economic costs to individuals and society related to lost work, increased school absenteeism, and decreased business revenues [1–4]. A pandemic influenza A(H1N1) vaccine became available in the USA in October 2009 [3]. Every year, approximately 36,000 people die from seasonal influenza or flu-related causes only in the USA [3]. Additionally, since there are thousands deaths worldwide due to the AH1N1/09 virus, it is important to understand the dynamics regarding the evolution of the AH1N1/09 virus.

The dynamic behavior of epidemic diseases has been studied for a long time since health is one of the most important issues in the real world. There are several approaches to study the dynamic of epidemics. One important branch are the models that include derivatives such as systems of ordinary differential equations. In these models, each equation may represent the number of individuals in the different stages. The most discussed type of infection spread is the SIR-system, in which individuals are susceptible (S), infective (I), or removed/immune (R), but there are others such as SI, SIS, SIR, SIRS, and SEIR [5, 6].

In order to study the dynamics of H1N1 influenza virus spread, several models have been presented. For instance, the classical SIR epidemiological model with a seasonal forced function has been used to model the influenza AH1N1/09 virus spread in the US population [7]. However, when considering influenza, the SEIR model, which is an immediate extension of the original SIR model, is more realistic. The SEIR model introduces a fourth compartment corresponding to the incubation (disease latency) stage when a person is infected but still not infectious enough to be able to transmit it. The SEIR model has been applied in epidemics that include a latency and recovery periods such dengue, influenza, rabies, and tuberculosis [5, 6, 8–10]. For instance, the SEIR model has been used to describe real

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data of tuberculosis, and the least squares fitting has been used for estimating the model parameters [9]. Furthermore, the SEIR model has been used to explore effective control and prevention measures for the human rabies in China, where it is one of the major public-health problems [10]. In regard to the influenza A(H1N1), the classical SEIR model has been used to predict the infected individuals, hospital bed shortage, and effectiveness of vaccination in a city of Japan and mixed with statistical methods in order to forecast the prevalence of A(H1N1) in Singapore [2, 11]. It is important to remark that while some parameters can be determined based on previous knowledge, other parameters must be estimated by fitting the model to the available data for the infected population. Thus, fitting epidemiological models to real data becomes a central problem for the field of infectious disease epidemiology [12–14].

Recently, fractional derivatives epidemic models have been used to deal with some epidemic behaviors [15–19]. An interesting study with a fractional model for the malaria has been developed in [20]. Additionally, fractional order models have been incorporated in several areas of science, engineering, applied mathematics, economics, and bioengineering, and consequently, considerable attention has been given to the solutions of fractional differential equations [21–27]. The application of fractional derivatives is in several cases justified because they provide a better model than integer order derivative models do. One advantage of the fractional order differential equation is that they provide a powerful instrument for incorporation of memory and hereditary properties of the systems as opposed to the integer order models, where such effects are neglected or difficult to incorporate. In addition, when fitting data, the fractional models has one more degree of freedom than the integer order model.

In this paper, we propose a nonlinear fractional order model in order to explain and understand the outbreaks of influenza A(H1N1) worldwide. In particular, we tested the proposed SEIR fractional order epidemic model with real data of the infected population of Bogotá City (Colombia) and of the Venezuelan Nueva Esparta state for the year 2009. The best value for the fractional order is estimated by minimizing the mean square error between the fractional model outputs and the real data of influenza A(H1N1). Thus, because the fractional epidemiological model includes another additional degree of freedom, we expect to obtain better results than with the classical SEIR model, but most important, the shape of the solutions agrees better with the data. It is important to mention that the nonlinear fractional model proposed here can be used in another regions to explain the outbreaks of influenza A(H1N1), but different parameters values may need to be used. Moreover, the SEIR fractional model may be used for different epidemics that follow the SEIR assumptions.

One important feature of fractional derivatives are that they are nonlocal opposed to the local behavior of integer derivatives. In this way, the next state of a fractional system depends not only upon its current state but also upon all of its historical states. In order to deal with fractional derivatives, we rely on the Caputo operator and on the Grünwald–Letnikov method to numerically approximate the fractional derivatives [28]. Even though various numerical approaches to different types of fractional diffusion models are increasingly appearing in the literature [28–34], we select this numerical method because it is computationally less expensive than others, and our main aim here is to test the fractional model and not to study the numerical methods for fractional differential equation systems [23, 28].

This paper is organized as follows. In Section 2, we present the basic definitions of fractional derivative and the Grünwald–Letnikov approximation. Section 3 is devoted to the presentation of SEIR fractional order epidemic model. In Section 4, we present the AH1N1/09 virus data and fit it using the classical and fractional SEIR epidemiological models. The last section is devoted to the conclusions.

2. Fractional derivatives

For many years, there have been several definitions that fit the concept of a noninteger order integral or derivative. The most famous of these definitions is the Riemann–Liouville. However, the most useful applications of fractional derivatives and integrals in engineering and science have been found only in the past one century. The mathematical notions have evolved in order to better meet the requirements of physical reality [28]. For instance, the Caputo fractional derivative, nowadays the most popular fractional operator among engineers and applied scientists, is obtained by reformulating the classical definition of Riemann–Liouville fractional derivative in order to make possible solution of the fractional initial value problems with standard initial conditions.

Here, we present the definition of fractional derivatives in the sense of Riemann–Liouville and Caputo. In addition, we present the Grünwald–Letnikov scheme based on finite differences. In order to simplify the basic definitions, we consider the interval $[0, T]$ instead of $[a, T]$ and omit $a = 0$ as an index in the differential operator. Suppose that the function $y(\tau)$ satisfies some smoothness conditions in every finite interval $(0, t)$ with $t \leq T$. Then, the Riemann–Liouville definition for fractional derivative is given by

$$ {}^{R}_{0}D^{\alpha}_{t}y(t) := \frac{1}{\Gamma(m-\alpha)}\frac{d^m}{dt^m}\int_0^t (t-\tau)^{-\alpha-1+m}y(\tau)d\tau \quad m-1<\alpha<m, \tag{1} $$

and the Caputo fractional derivative is defined as follows:

$$ {}^{C}_{0}D^{\alpha}_{t}y(t) := \frac{1}{\Gamma(m-\alpha)}\int_0^t (t-\tau)^{-\alpha-1+m}\frac{d^m}{d\tau^m}y(\tau)d\tau \quad m-1<\alpha<m, \tag{2} $$

where α is the order of the derivative. These two definitions are not equivalent to each other, and their difference is expressed by

$$ {}^{C}_{0}D^{\alpha}_{t}y(t) = {}^{R}_{0}D^{\alpha}_{t}y(t) - \sum_{\nu=0}^{m-1} r^{\alpha}_{\nu}(t)y^{(\nu)}(0),\ r^{\alpha}_{\nu}(t) = \frac{t^{\nu-\alpha}}{\Gamma(\nu+1-\alpha)}. \tag{3} $$

The Caputo operator ${}_0^C D_t^\alpha$ has advantages for differential equations with initial values. In the case of Riemann–Liouville and Caputo derivatives, respectively, the initial values are usually given as

$$ {}_0^R D_t^\alpha y(0) = b_\nu, \quad {}_0^C D_t^\alpha y(0) = b_\nu, \ \ \nu = 1, 2, \ldots, m. \tag{4} $$

A direct definition of the fractional derivative $D_t^\alpha y(t)$ is based on finite differences of an equidistant grid in $[0, t]$. Assume that the function $D_t^\alpha y(\tau)$ satisfies some smoothness conditions in every finite interval $(0, t)$, $t \leq T$. Choosing the grid

$$ 0 = \tau_0 < \tau_1 < \ldots < t = \tau_{n+1} = (n+1)h, \ \ \tau_{n+1} - \tau_n = h, \tag{5} $$

and using the classical notation of finite differences,

$$ \frac{1}{h^\alpha} \Delta_h^\alpha y(t) = \frac{1}{h^\alpha} \left(y(\tau_{n+1}) - \sum_{\nu=1}^{n+1} c_\nu^\alpha y(\tau_{n+1-\nu}) \right), \tag{6} $$

where

$$ c_\nu^\alpha = -(1)^{\nu-1} \binom{\alpha}{\nu}, \tag{7} $$

and the Grünwald–Letnikov definition reads [28, 35]

$$ D_t^\alpha y(t) = \lim_{h \to 0} \frac{1}{h^\alpha} \Delta_h^\alpha y(t). \tag{8} $$

In a sense, Grünwald–Letnikov is an extension of the Euler method to fractional differential equations. If we take the limit $\alpha \to 1$, then the classical explicit or implicit Euler method is obtained. Compared with linear multistep methods, the sum of divided differences becomes longer and longer [28, 35]. Let us now apply the Grünwald–Letnikov definition to the following fractional differential equation using the Caputo operator

$$ {}_0^C D_t^\alpha y(t) = f(y(t)), \ \ y(\tau) = y_0 \ \ (0 < \alpha < 1) \tag{9} $$

and assume that there exists a unique solution $y = y(\tau)$ in the interval $[0, T]$ and let y_k denote the approximation of the true solution $y(\tau_k)$. Then, the explicit or implicit Grünwald–Letnikov method for an equidistant grid is given by

$$ y_{n+1} - \sum_{\nu=1}^{n+1} c_\nu^\alpha y_{n+1-\nu} - r_{n+1}^\alpha y_0 = h^\alpha f(y_n) \ \text{ or } \ h^\alpha f(y_{n+1}). \tag{10} $$

3. SEIR fractional differential model

In this section, we present the SEIR epidemic fractional differential model. First, we introduce the classical SEIR model. The SEIR epidemiological model considers that the total population $N(t)$ is divided into four subpopulations: $S(t)$ susceptible, $E(t)$ people incubating the virus, infectious $I(t)$, and recovered $R(t)$ subpopulations. In addition, we consider that newborn children become susceptible at a rate μ (birth rate), and individuals leave the system by death at a rate d. An individual in $S(t)$ flows to $E(t)$ because people in $I(t)$ transmit A(H1N1) virus by effective contacts at rate β. Finally, we consider that once an individual is recovered, he or she acquires permanent immunity [3]. The other parameters of the model are ρ, recovery rate from the infection and latent individuals become infected at rate Ω. The population-scaled SEIR model (without loss of generality) with constant population size ($d = \mu$) is given by

$$ \begin{aligned} \dot{S}(t) &= \mu - \mu S(t) - \beta S(t) I(t), \\ \dot{E}(t) &= \beta S(t) I(t) - (\mu + \Omega) E(t), \\ \dot{I}(t) &= \Omega E(t) - (\mu + \rho) I(t), \\ \dot{R}(t) &= \rho I(t) - \mu R(t). \end{aligned} \tag{11} $$

Let us now consider the SEIR fractional model using the first-order Caputo derivatives of order α and given by the following nonlinear system,

$$ \begin{aligned} {}_0^C D_t^\alpha S(t) &= \mu^\alpha - \beta^\alpha S(t) I(t) - \mu^\alpha S(t), \\ {}_0^C D_t^\alpha E(t) &= \beta^\alpha S(t) I(t) - (\mu^\alpha + \Omega^\alpha) E(t), \\ {}_0^C D_t^\alpha I(t) &= \Omega^\alpha E(t) - (\mu^\alpha + \rho^\alpha) I(t), \\ {}_0^C D_t^\alpha R(t) &= \rho^\alpha I(t) - \mu^\alpha R(t), \end{aligned} \tag{12} $$

where the parameters of the model are analogous to those of model (11), and $S(t)+E(t)+I(t)+R(t)=1$, $(S,E,I,R)\in\mathbb{R}^4_+$, where

$$\mathbb{R}^4_+=\left\{X\in\mathbb{R}^4 : X\geq 0\right\},$$

with $X(t)=(S(t),E(t),I(t),R(t))^T$, and $0<\alpha\leq 1$. However, it is important to notice that these modified parameters, such as β^α, depend on the fractional order and that the units of the differential equation are different.

The SEIR model has many variants that include births, deaths, seasonal transmission rates, or stochastic components [5,6]. It is important to remark that when $\alpha\to 1$ the fractional epidemic model (12) reduces to the classical SEIR epidemiological model, but that in certain cases an order different from one makes the fractional model more realistic [36].

4. Nonnegative solutions

For the proof of the theorem about nonnegative solutions, we need the following Lemma [37]:

Lemma 1 (Generalized mean value theorem)
Let $f(x)\in C[a,b]$, and ${}_0^C D_t^\alpha f(x)\in C(a,b]$, for $0<\alpha\leq 1$. Then, we have that

$$f(x)=f(a)+\frac{1}{\Gamma(\alpha)}\,{}_0^C D_t^\alpha f(\xi)(x-a)^\alpha,$$

with $0\leq\xi\leq x$, $\forall x\in(a,b]$.

Remark 4.1
If $f(x)\in C[0,b]$ and ${}_0^C D_t^\alpha f(x)\in C(0,b]$ for $0<\alpha\leq 1$, it is clear that from Lemma 1 that if ${}_0^C D_t^\alpha f(x)\geq 0$, $\forall x\in(0,b)$, then the function f is nondecreasing, and if ${}_0^C D_t^\alpha f(x)\leq 0$, $\forall x\in(0,b)$, then the function f is nonincreasing for all $x\in[0,b]$.

Theorem 4.2
There is a unique solution for the initial value problem given by (12), and the solution remains in $\mathbb{R}^4_+$.

Proof
The existence and uniqueness of the solution of (12) in $(0,\infty)$ follow from the results given in [38]. Now, we need to show that the domain $\mathbb{R}^4_+$ is positively invariant.

$$\begin{aligned}
{}_0^C D_t^\alpha S|_{S=0}&=\mu^\alpha>0,\\
{}_0^C D_t^\alpha E|_{E=0}&=\beta^\alpha SI\geq 0,\\
{}_0^C D_t^\alpha I|_{I=0}&=\Omega^\alpha E\geq 0,\\
{}_0^C D_t^\alpha R|_{R=0}&=\rho^\alpha I\geq 0.
\end{aligned}$$

Thus, on each hyperplane bounding the nonnegative orthant, the vector field points into $\mathbb{R}^4_+$. □

5. Local stability analysis of model

By setting the right-hand side of the system (12) equal to zero, one obtains that the equilibrium points are given by $P_F=(1,0,0,0)$, and $P_E=(S^*,E^*,I^*,R^*)$, where

$$S^*=\frac{(\mu^\alpha+\Omega^\alpha)(\mu^\alpha+\rho^\alpha)}{\beta^\alpha\Omega^\alpha},\ E^*=\frac{\mu^\alpha-\mu^\alpha S^*}{\Omega^\alpha+\mu^\alpha},\ I^*=\frac{\Omega^\alpha E^*}{\rho^\alpha+\mu^\alpha},\ R^*=\frac{\rho^\alpha I^*}{\mu^\alpha}.$$

The Jacobian matrix $J(P_F)$ for the system given in (12) evaluated at the disease free equilibrium is

$$J(P_F)=\begin{pmatrix}
-\mu^\alpha & 0 & -\beta^\alpha & 0\\
0 & -\mu^\alpha-\Omega^\alpha & \beta^\alpha & 0\\
0 & \Omega^\alpha & -\mu^\alpha-\rho^\alpha & 0\\
0 & 0 & \rho^\alpha & -\mu^\alpha
\end{pmatrix}.$$

The disease free equilibrium is asymptotically stable if all of the eigenvalues, λ_i for $i=1,2,3,4$ of $J(P_F)$ satisfies the following condition [39,40]

$$|\arg\lambda_i|>\alpha\frac{\pi}{2}. \tag{13}$$

These eigenvalues can be determined by solving the characteristic equation

$$det(J(P_F)-\lambda I)=0.$$

A quick calculation, allow us to obtain the following algebraic equation

$$(\lambda+\mu)^2(\lambda^2+(2\mu+\Omega+\rho)\lambda+(\mu+\rho)(\mu+\Omega)-\beta\Omega)=0.$$

Therefore, $\lambda_{1,2}=-\mu^\alpha$. Setting $A=\mu^\alpha+\rho^\alpha$, $B=\mu^\alpha+\Omega^\alpha$, $C=\beta^\alpha\Omega^\alpha$, one obtains $\lambda^2+(A+B)\lambda+(A\cdot B-C)=0$. The roots of this equation given by

$$\lambda_{3,4}=\frac{-(A+B)\pm\sqrt{(A+B)^2-4(AB-C)}}{2},$$

and because $A+B>0$, then if $AB>C$, all of the eigenvalues λ_i for $i=1,2,3,4$ satisfy the condition given by (13). Therefore, all the eigenvalues have negative real parts if $\mathcal{R}_0=\frac{\Omega^\alpha\beta^\alpha}{(\Omega^\alpha+\mu^\alpha)(\mu^\alpha+\rho^\alpha)}<1$. Thus, we conclude that

Theorem 5.1
The disease free equilibrium P_F of the system (12) is asymptotically stable if $\mathcal{R}_0<1$.

6. AH1N1/09 virus data and model fitting using SEIR epidemiological model

The reported cases of pandemic AH1N1/09 influenza represent those who tested positive to influenza A virus using laboratory testing, and the data are reported by weeks. The data were originally collected from state health institutions were individuals presenting acute symptoms were attended. The reported dates correspond to when the samples were taken. The influenza A(H1N1) tests were performed using specimens from nasal swabs or aspirates and uses real-time reverse transcription polymerase chain reaction or viral culture. In Table I, we can see the number of registered people who tested positive in the metropolitan area of Bogotá D.C. (Colombia). As can be observed, the highest number of positive reported cases of AH1N1/09 influenza was in the 34th week of 2009. The reported positive cases of pandemic AH1N1/09 influenza in the Venezuelan state of Nueva Esparta are presented in Table II. Again, the highest number of positive reported cases was in the 34th week of 2009.

In order to adjust the SEIR model (11) to time-series data of confirmed cases of pandemic AH1N1/09 influenza, we need to set some parameters values. Unfortunately, the epidemiology of pandemic AH1N1/09 virus is not accurately known. The parameter values were chosen based on the best available data. The incubation period for pandemic AH1N1/09 virus has been reported to be 2–10 days with a mean of 6 days [1]. Therefore, the mean time in the exposed classes $E(t)$ has been assumed to be $\Omega=\frac{1}{5}$ days^{-1}. The infectious period has been reported between 4 and 7 days with $\rho=\frac{1}{7}$ days^{-1} [41,42]. It is important to remark that each one of the parameters μ, Ω, ρ, and β can be interpreted as the mean of the length of the transit period between two subpopulations. Therefore, the earlier numerical values computed for each parameter should be considered as the average length of transition periods between two subpopulations and should not be regarded as a fixed time after which each individual crosses to a new subpopulation. Additionally, since we use the SEIR model for a relatively short period, we assume a constant population size. Therefore, the birth and death rate are assumed equal and $\mu=d=\frac{0.015}{52}$ days^{-1}, which means a life expectancy of approximately 70 years.

It is important to remark that unfortunately, time-series data of confirmed cases of pandemic AH1N1/09 influenza do not correspond exactly to subpopulation $I(t)$, because only a fraction s(scale factor) still to be determined of people who feel sick decide to go to a doctor who then reported the case. In this way, the only parameters that need to be estimated by a fitting process to real data are the influenza AH1N1 transmissibility β, the fractional order α, and the scale factor s. The parameter β is the product of the susceptibility of the population, the infectivity of the disease, and the number of contacts an individual has in a day. The initial conditions,

Table I. Data provided by the Secretaria de Salud Distrital de Bogotá D.C. First row corresponds to week number of year 2009. Second row shows the number of infectious individuals by AH1N1/09 detected in each week because those people went to see a doctor and were reported and controlled.

Week	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Cases	4	1	0	1	2	5	12	17	22	16	15	53	55	45
Week	31	32	33	34	35	36	37	38	39	40	41	42	43	44
Cases	84	102	127	261	210	155	109	116	125	76	52	19	15	1

Table II. Data provided by the National Health Department of Venezuela . First row corresponds to week number of year 2009. Second row shows the number of infectious by AH1N1/09 detected in each week because these people went to see a doctor and were reported. Data about deaths are not available.

Week	24	25	26	27	28	29	30	31	32	33	34	35	36	37
Cases	2	3	0	0	1	1	3	0	2	1	13	9	8	1
Week	38	39	40	41	42	43	44	45	46	47	48	49	50	
Cases	5	2	2	1	0	0	0	1	0	0	1	0	0	

t_0, $S(t_0)$, $E(t_0)$, $I(t_0)$, and $R(t_0)$, are also unknown. However, because our research focuses on qualitative results rather than in quantity, and small changes on the initial conditions do not modify the qualitative behavior, we set the initial conditions $S(t_0) = 1 - 0.001$, $I(t_0) = 0.001$, $E(t_0) = 0$, and $R(t_0) = 0$, which means that a small fraction of the population is initially infected.

A fitting process is performed to estimate α, β, and the scale factor s by least squares method and using Nelder–Mead algorithm [43]. Notice that this process has higher computational requirements because the fractional order model is more demanding computationally than the classical integer order model. In order to compute the best fitting, we implemented the function

$$\begin{array}{rccc} \mathbb{F} & : & \mathbb{R}^3 & \longrightarrow & \mathbb{R} \\ & & (\alpha, \beta, s) & \longrightarrow & \mathbb{F}\,(\alpha, \beta, s) \end{array}$$

where α, β, and s are variables such that

(1) For a given (α, β, s), solve numerically the system of differential equations (11) and obtain a solution $\hat{Y}_i(t) = (\hat{S}_i(t), \hat{E}_i(t), \hat{I}_i(t), \hat{R}_i(t))$, which is an approximation of the real world solution $Y(t)$.

(2) Set $t_0 = 16$ (the fitting process starts at week 16) and for $t = 17, 18, \ldots, 44$ (Bogotá D.C.), corresponding to weeks where data are available, evaluate the computed numerical solution for subpopulation $I(t)$; that is, $\hat{I}(17), \hat{I}(18), \hat{I}(19), \ldots, \hat{I}(44)$.

(3) Compute the root mean square of the difference between $\hat{I}(17), \hat{I}(18), \hat{I}(19), \ldots, \hat{I}(44)$ (Bogotá D.C.) and infectious data in Table I. This function $\mathbb{F}$ returns the root mean square value (*RMS*), where for the Bogotá D.C. data are given by

$$RMS = \sqrt{\sum_{j=0}^{27} (\hat{I}(17+j) - I(17+j))^2}.$$

(4) Find a global minimum for the RMS using Nelder–Mead algorithm.

The function $\mathbb{F}$ takes values in $\mathbb{R}^3$ and returns a positive real number, the root mean square that measures the closeness of the scaled infectious population, provided by the model, to time-series data. Hence, we can try to minimize this function using the Nelder–Mead algorithm [43] that does not involve the computation of any derivatives or gradients, impossible to know for function $\mathbb{F}$. In order to find a global minimum, we take 500 initial different points for the Nelder–Mead algorithm in the domain $[0.01, 0.999] \times [0, 10] \times [0, 10^5] \subset \mathbb{R}^3$. We stored all the minima obtained and, among them, the values of α, β, and s that minimize the function $\mathbb{F}$. In other words, the Nelder–Mead algorithm return the best values of α, β, and s, which give the minimum of the RMS.

7. Numerical simulations of the SEIR fractional epidemic model

Analogously to the classical theory of differential equations, there are no general methods to solve systems of fractional differential equations analytically. Furthermore, the fractional case is more difficult to handle even numerically [44]. Several methods based on a continuous expansion formula for the fractional derivative have been proposed where in some cases the use classical methods can be applied to obtain an approximate solution to the original fractional order model.

In this section, numerical results for the solution of the SEIR epidemic fractional model are presented. Because no analytical solution to the nonlinear fractional system (12) is available, we use the Grünwald–Letnikov method described earlier to compute the solution numerically. The data from metropolitan area of Bogotá D.C. (Colombia) related to A(H1N1) are from weeks 17 to 44. On the other hand, the data of Venezuelan Nueva Esparta state is from weeks 24 to 50. The time step size has been chosen as $\Delta t = 0.01$ days. However, other computations with smaller time step sizes were performed, but the results do not give significant differences.

First, in order to observe the effects that the parameters α and β have on the dynamics of the AH1N1/09 influenza epidemic, we include several numerical simulations varying the values of these parameters. On the left-hand side of Figure 1, the dynamics varying the parameter α can be seen . The numerical results show that for lower values of α, the epidemic peak is wider and lower. This feature is important from a health point of view since it translates to a longer period in which infected individuals can affect the health system. Notice that the profile of the epidemics are not longer symmetrical, which can be more realistic for some epidemics. In regard to the effect of the parameter β, it can be observed on the right-hand side of Figure 1 that for lower values of β, the epidemic peak is lower, and the epidemic develops more slowly. In this way, the combination of the parameters α and β of the SEIR fractional model allows to produce a better fit to the real epidemic data of different diseases that follow the SEIR flow.

Next, the proposed fractional model is fitted to the known real data related to A(H1N1) infected cases. In order to fit the fractional model, we have solved our nonlinear fractional system (12) with different values for the parameters α, β^α, and the factor scale s. We have used values for α in the interval $[0.01, 1]$ spaced by 0.01 and for $\beta^\alpha = 4.1$ in the interval $[0.01, 10]$ spaced by 0.1. The best nonlinear fractional model in regard to the mean square error for the real data of people infected with A(H1N1) in Bogotá D.C. is obtained using $\alpha = 0.88$, $\beta^\alpha = 4.1$, and $s = 1490$. In Figure 2, the fitting of the classical model (11) on the left-hand side and the nonlinear fractional model (12) to the time-series data of confirmed cases of pandemic AH1N1/09 influenza from Bogotá D.C. can be seen graphically. It can be observed that the fractional model (12) produces a epidemic peak that adjust better with the peak of the real data. It is important to mention that the SEIR fractional model generates epidemic data that fits better than the classical SEIR model in terms of the mean square error. The SEIR fractional model gives a wider peak, which allows to obtain a more accurate fitting. A wider epidemic peak translates to a longer period in which a high number of infected individuals can overcrowd the health system. Another option to obtain wider peaks in the solution values for the infected population is to modify the parameter values of ρ and Ω. However, in this case,

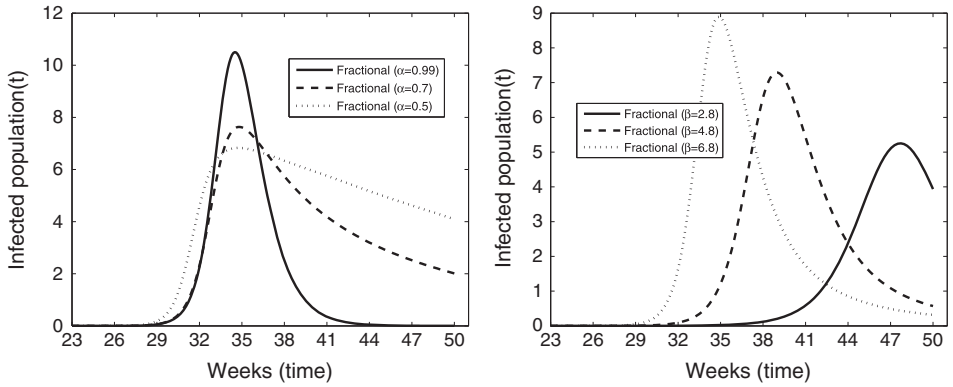

Figure 1. Numerical solution of the classical SEIR model varying the value of α and using a fixed value for $\beta^{\alpha} = 6.8$ (Left). Numerical solution of the SEIR model fractional varying the value of β^{α} and using a fixed value for $\alpha = 0.9$ (Right).

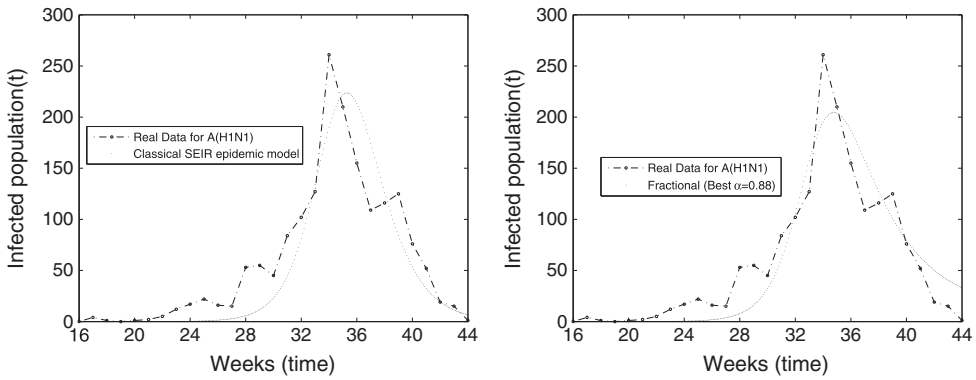

Figure 2. Numerical solution of the classical SEIR model adjusted to real data of people infected with A(H1N1) Bogotá D.C. (Colombia) (Left). Numerical solution of the SEIR model fractional adjusted to real data of people infected with A(H1N1) in Bogotá D.C. (Colombia), with $\alpha = 0.88$ and $\beta^{\alpha} = 4.1$ (Right).

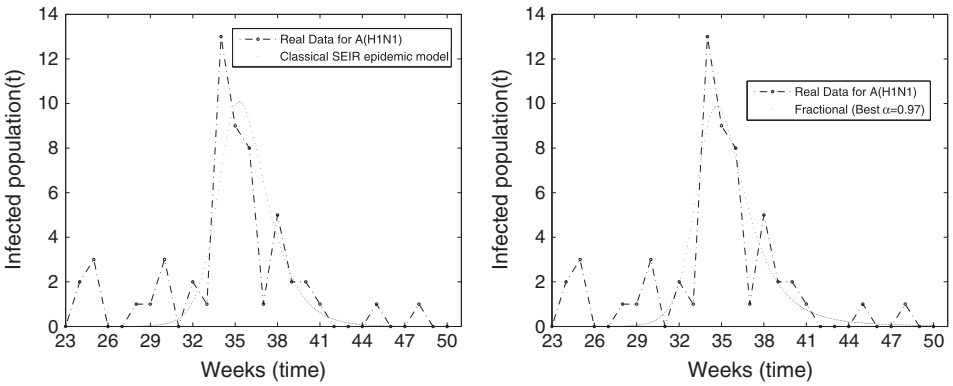

Figure 3. Numerical solution of the classical SEIR model adjusted to real data of people infected with A(H1N1) for Venezuelan Nueva Esparta state (Left). Numerical solution of the SEIR model fractional adjusted to real data of people infected with A(H1N1) for Venezuelan Nueva Esparta state, with $\alpha = 0.97$ and $\beta^{\alpha} = 6.8$ (Right).

we may obtain unrealistic profiles because we are taking unreal parameter values regarding the incubation and recovery period of the influenza A(H1N1).

The best nonlinear fractional model in regard to the mean square error for the data of the Venezuelan Nueva Esparta state is obtained using $\alpha^{\alpha} = 0.97$, $\beta^{\alpha} = 6.8$, and $s = 46$. In Figure 3, the fitting of the classical model (11) on the left-hand side and the nonlinear fractional model (12) to the time-series data of confirmed cases of pandemic AH1N1/09 influenza from the Venezuelan Nueva Esparta state can be observed graphically . As in the case of Bogotá D.C., the SEIR fractional epidemic model (12) produces a epidemic peak that adjust better with the peak of the real epidemic data and the mean square error is lower than with the classical model.

8. Conclusions

In this paper, we proposed a nonlinear fractional order model in order to explain and understand the outbreaks of influenza A(H1N1) worldwide. In the fractional model, the next state depends not only upon its current state but also upon all of its historical states. In order to deal with the fractional derivatives of the model, we rely on the Caputo operator and on the Grünwald–Letnikov method to approximate the fractional derivatives.

We tested the proposed SEIR fractional order model with real data for the infected population of Bogotá City (Colombia) and from the Venezuelan Nueva Esparta state for the year 2009. The parameter values of the model were estimated minimizing the mean square error between the fractional model outputs and the real data of influenza A(H1N1). We found that the proposed fractional model epidemic peak adjusts better to the peak of the real data and gives better results in terms of the mean square error than with the classical SEIR epidemic model. In addition, it can be seen that the fractional model gives wider peaks and leads to better approximations for the real epidemic data of Bogotá City (Colombia) and from the Venezuelan Nueva Esparta state. This fact is important from a health point of view since it translates to a longer period with a high number of infected individuals, which can affect the health system.

Finally, it is important to mention that the SEIR nonlinear fractional model can be used in another regions to explain the outbreaks of influenza A(H1N1), but different parameter values may need to be used. It is concluded that the fractional order epidemic model produces numerical results that agree very well with the real data of influenza A(H1N1). Moreover, the model can provide useful information for the understanding, prediction, and control of the transmission of different epidemics that follow the SEIR structure flow. It is also important to notice that mathematical models based on fractional differential equations are in many cases a more powerful approach to epidemiological models, because one can choose the order α of fractional differentiation that best corresponds to real data.

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