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Numerical Modeling of the Transmission Dynamics of Influenza

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Abstract A deterministic mathematical model for the transmission dynamics of Influenza is studied. Although the equilibria of the model could not be expressed in closed form, their existence and threshold conditions for their stability are theoretically investigated. It is shown that the disease-free equilibrium is locally–asymptotically stable if the basic reproductive number $R_0 < 1$ (thus, Influenza can be eradicated from the community) and unstable if $R_0 > 1$ (leading to the persistence of Influenza within the community). A competitive finite-difference method will be constructed and used for the solution of the resulting system of first-order, non-linear, initial-value problem (IVP). Unlike the fourth-order Runge-Kutta method (RK4), which fails when the discretization parameters exceed certain values, the novel numerical method to be developed in this paper gives convergent results for all parameter values. The introduction of seasonal variation into the model leads to periodic and chaotic dynamics of epidemics which are present in the numerical simulations.

Keywords Influenza; Equilibria; Stability; Finite-difference method

1 Introduction

Influenza is caused by a virus that can be of three different types (A, B and C, see [13]). Among these types, the virus A is epidemiologically the most important for humans, since it can recombine its genes with those of strains circulating in animal populations (birds, swine and horses). These relatively rare recombinations give rise every few decades to new viral subtypes via the so called antigenic shift mechanism [15]. Much evidence [4,15] shows that the antigenic distance between two different strains influences the degree of partial immunity, often called cross-immunity, and conferred to a host already infected by one of the strains with respect to the other.

Many mathematical models have been proposed in the literature to describe the inter-pandemic ecology of influenza A in humans (see [5] for a review). Andreasen et al. [2] and Lin et al.[11] developed epidemiological models to shown that multiple strains of influenza can persist in the human populations and that their prevalence can exhibit self-sustained oscillations through time. Pease [13] studied the emergence of new viral strains is that of introducing into the model a loss of immunity by the host. Gill and Murphy [6] showed that the probability of recovered individuals being reinfected by new circulating strains linearly increases with the time since last infection.

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Casagrandi [3] introduced a new compartment C in the population, which can be called cross-immune, to design an intermediate state between the fully susceptible state $(S)$and the fully protected one(R). Kermack and McKendrick [9] introduced epidemic models of temporary partial immunity – or variable susceptibility and have recently been studied in the context of influenza [8]. Most of these studies, however, appear to give scant or no detail of the numerical methods used, together with their associated stability analyses, to solve the resulting initial value problems (IVPs).

It is well-known that solving nonlinear IVPs with explicit finite-difference methods such as Euler and Runge-Kutta methods can result in contrived chaos and oscillations for certain values of the discretization parameters [7,10,14]. Although such scheme-dependent numerical instabilities can often be avoided by using small time-steps, the extra computing cost incurred when examining the long-term behavior of a dynamical system may be substantial. To circumvent contrived chaos and other scheme dependent numerical instabilities, implicitly-derived schemes with certain additional desired properties are generally preferred.

It is the purpose of the present paper to present a simple finite-difference numerical method for the solution of the so-called *SIRC* (susceptible/infectious/recovered/ cross-immune) model of influenza dynamics [3]. The method is first order, the same as the well-known Euler method. Although implicit by construction, the method can be implemented explicitly. The *SIRC* model with forcing is known to lead to more complex oscillatory and chaotic behavior. In this paper, the dynamics of the *SIRC* model with seasonal forcing using the proposed method are analyzed and tested in numerical simulations.

The *SIRC* model is depicted in the compartment diagram, Fig. 1, and is expressed as the initial-value problem

$$\begin{aligned}
\frac{dS}{dt} &= \mu(1-S)+\gamma C-\beta SI,\\
\frac{dI}{dt} &= \beta SI+\sigma\beta CI-(\mu+\alpha)I,\\
\frac{dR}{dt} &= (1-\sigma)\beta CI+\alpha I-(\mu+\delta)R,\\
\frac{dC}{dt} &= \delta R-\beta CI-(\mu+\gamma)C.
\end{aligned} \tag{1}$$

in which $S = S(t)$, $I = I(t)$, $R = R(t)$ and $C = C(t)$ represent the proportions of susceptible, infectious, recovered and cross-immune, respectively, and a prime denotes differentiation with respect to time, t. The model assumes a population of constant size, N, so that $N = S+I+R+C$. Table 1 provides an interpretation of the model parameters. Further details on the biological motivation and the associated assumptions are given in [3].

	Definitions	Values
μ	The mortality rate	$0.02\ \mathrm{y}^{-1}$
α	Rate of progression from infective to recovered per year	$365/3\ \mathrm{y}^{-1}$
δ	Rate of progression from recovered to cross-immune per year	$0.625\ \mathrm{y}^{-1}$
γ	Rate of progression from recovered to susceptible per year	$0.35\ \mathrm{y}^{-1}$
σ	The recruitment rate of cross-immune into the infective	$0 \leq \sigma \leq 1$
β	Contact rate per year	1200
ε	Degree of seasonality	$0 \leq \varepsilon \leq 1$

Table 1: Model parameters

2 Analysis of the model

In this section, the model (1) will be qualitatively analyzed to investigate the existence and stability of its associated equilibria.

2.1 Disease-free equilibrium

In the absence of infection (that is, $I = 0$), the model has a disease-free equilibrium $P0 = (1,0,0,0)$ which is obtained by setting the right-hand sides of (1) to zero. To establish the stability of this equilibrium, the Jacobian of (1) is computed and evaluated at P^0. The local stability of P^0 is then determined based on the signs of the eigenvalues of this Jacobian. The equilibrium P^0 is locally asymptotically stable if the real parts of these eigenvalues are all negative. The Jacobian of (1) at P^0 is

$$J(P^0) = \begin{bmatrix} -\mu & -\beta & 0 & \gamma \\ 0 & \beta-(\mu+\alpha) & 0 & 0 \\ 0 & \alpha & -(\mu+\delta) & 0 \\ 0 & 0 & \delta & -(\mu+\gamma) \end{bmatrix}$$

with eigenvalues $\lambda_1 = -\mu,\ \lambda_2 = -(\mu+\delta),\ \lambda_3 = -(\mu+\gamma)$and $\lambda_4 = \beta-(\mu+\alpha)$.

Let $R_0 = \frac{\beta}{\mu+\alpha}$, thus $\lambda_4 < 0$if and only if $R_0 < 1$. Since λ_i, $i = 1,2,3,4$ are negative (since all model parameters are assumed to be positive), the infection-free equilibrium P^0 is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. The quantity R_0 is called the basic reproductive number of infection []. In the context of epidemiological modeling (see [1]), it is generally known that if $R_0 < 1$, then the disease-free equilibrium is locally asymptotically stable (and the disease will be eradicated from the community if the initial sizes of the four state variables are within the vicinity of P^0). If the equilibrium P^0 is globally asymptotically stable, then the disease will be eradicated from the population irrespective of the initial sizes of the four state variables. Therefore, in the event of an epidemic, the theoretical determination of conditions that can make R_0 less than unity is of great public health interest.

2.2 Endemic equilibrium

In the presence of infection ($I \neq 0$), model (1) has a unique endemic equilibrium given by $P^* = (S^*,\ I^*,\ R^*,\ C^*)$ where

$$\begin{aligned} S^* &= \frac{\mu+\alpha}{\beta} - \sigma\left[\frac{\delta\alpha I^*}{[(\mu+\delta)-(1-\sigma)\delta]\beta I^* + (\mu+\gamma)(\mu+\delta)}\right], \\ R^* &= \frac{\alpha I(\beta I^* + \mu + \gamma)}{[(\mu+\delta)-(1-\sigma)\delta]\beta I^* + (\mu+\gamma)(\mu+\delta)}, \\ C^* &= \frac{\delta\alpha I^*}{[(\mu+\delta)-(1-\sigma)\delta]\beta I^* + (\mu+\gamma)(\mu+\delta)}, \end{aligned}$$

and I^* is the root of the equation $aI^2 + bI + c = 0$where

$$\begin{aligned} a &= \beta\mu^2 + \alpha\mu\beta + \mu\sigma\delta\beta, \\ b &= \beta\mu\{\alpha(2\mu+\delta+\gamma) + (\mu+\gamma)(\mu+\delta) + \mu(\mu+\sigma\delta) - \beta(\mu+\sigma\delta)\}, \\ c &= \mu(\mu+\gamma)(\mu+\delta)(\mu+\alpha)(1-R_0). \end{aligned}$$

It is found that a is positive independently of the parameter values and $c$is negative if and only if$R_0 > 1$. Given these constraints, the positivity and uniqueness of P^* are guaranteed if and only if $R_0 > 1$. Evaluating the Jacobian of (1) at P^* gives the characteristic polynomial: $\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0$

where $a_1 = 3\mu + \alpha + \gamma + 2\beta I^*$,

$$\begin{aligned} a_2 &= \mu(\mu+\gamma+\beta I^*) + \alpha(\mu+\gamma) + \beta I^*[\alpha - \delta(1-\sigma)] \\ &\quad + (\mu+\beta I^*)(2\mu+\alpha+\gamma+\beta I^*) + \beta^2 S^* I^* + \sigma\beta^2 I^* C^*, \\ a_3 &= (\mu+\beta I^*)[(\mu+\alpha)(\mu+\gamma) + \beta I^*(\mu+\alpha-\delta(1-\sigma))] \\ &\quad + \beta^2 S^* I^*(2\mu+\gamma+\beta I^*) \quad + \beta^2 I^* C^*(\gamma + \sigma(\mu+\beta I^*)) \\ &\quad + \sigma\beta^2 I^* C^*[\mu+\alpha-\delta(1-\sigma)] + \alpha\beta I^*(\beta S^* - \delta\sigma), \\ a_4 &= \beta^2 I^*[\mu+\alpha-\delta(1-\sigma)][\beta S^* I^* + C^*(\gamma+\sigma(\mu+\beta I^*))] \\ &\quad + \beta I^*[\beta S^*(\mu+\alpha)(\mu+\gamma) - (\gamma+\sigma(\mu+\beta I^*))\delta\alpha]. \end{aligned}$$

Using Routh–Hurwitz stability criteria [10], the endemic equilibrium P^* is locally asymptotically stable provided

$a_i > 0,\ i = 1,2,3,4, \quad a_1a_2 - a_3 > 0$and $a_1a_2a_3 - a_1^2a_4 - a_3^2 > 0$.

3 The numerical method

The time variable $t \geq 0$ will be discretized at the points $t_n = n\ell$ $(n = 0,1,2,...)$ where $\ell > 0$ is a constant time step. The solutions of (1) at the point t_n are $S(t_n)$, $I(t_n)$, $R(t_n)$ and $C(t_n)$. The solutions of the numerical method at the same point t_n will be denoted by S^n, I^n, R^n and C^n, respectively. Starting with the IVP for S in (l), first of

all, the development of numerical methods may be based on approximating the time derivative by its first-order forward-difference approximant given by

$$\frac{dS(t)}{dt} = \frac{1}{\ell}[S(t+\ell) - S(t)] + O(\ell) \text{ as } \ell \to 0,$$

in which $t = t_n$. The implicit first-order method for solving S in (1) is given by

$$\frac{1}{\ell}[S^{n+1} - S^n] = \mu(1 - S^{n+1}) - \beta S^{n+1} I^n + \gamma C^n, \tag{2}$$

Similarly, the following are implicit methods for I, R and C respectively:

$$\frac{1}{\ell}[I^{n+1} - I^n] = \beta S^{n+1} I^n + \sigma\beta C^n I^n - (\mu + \alpha) I^{n+1}, \tag{3}$$

$$\frac{1}{\ell}[R^{n+1} - R^n] = (1-\sigma)\beta C^n I^{n+1} + \alpha I^{n+1} - (\mu + \delta) R^{n+1}, \tag{4}$$

$$\frac{1}{\ell}[C^{n+1} - C^n] = \delta R^{n+1} - \beta C^{n+1} I^{n+1} - (\mu + \gamma) C^{n+1}, \tag{5}$$

Rearranging the methods (2)-(5) give

$$\begin{aligned} S^{n+1} &= \frac{S^n + \ell\mu + \ell\gamma C^n}{1 + \ell(\mu + \beta I^n)}, \; I^{n+1} = \frac{I^n + \ell\beta S^{n+1} I^n + \ell\sigma\beta C^n I^n}{1 + \ell(\mu + \alpha)}, \\ R^{n+1} &= \frac{R^n + \ell(1-\sigma)\beta C^n I^{n+1} + \alpha\ell I^{n+1}}{1 + \ell(\mu + \delta)}, \; C^{n+1} = \frac{C^n + \ell\delta R^{n+1}}{1 + \ell(\beta I^{n+1} + \mu + \gamma)}. \end{aligned} \tag{6}$$

This method, (6), is denoted by DSS1 method. It should be noted that the method {(2)-(5)} is implicit by construction, the numerical result is obtained explicitly by solving a linear algebraic system at every time-step using (6). Furthermore, it is clear that none of the discrete schemes (6) has negative terms on their right-hand sides for $0 < \sigma < 1$. Thus, the discrete scheme (6) satisfies the positivity property, and hence will not be expected to exhibit numerical instabilities.

The associated local truncation errors of DSS1 method are, respectively,

$$\begin{aligned} L_S &= [1 + \ell(\mu + \beta I(t))] S(t+\ell) - S(t) - \ell\gamma C(t) - \ell\mu, \\ L_I &= [1 + \ell(\mu + \alpha)] I(t+\ell) - [1 + \ell\beta S(t+\ell) + \ell\sigma\beta C(t)] \; I(t), \\ L_R &= [1 + \ell(\mu + \delta)] R(t+\ell) - R(t) - [(1-\sigma)\ell\beta C(t) + \ell\alpha] I(t+\ell), \\ L_C &= [1 + \ell\beta I(t+\ell) + \ell(\mu + \gamma)] C(t+\ell) - C(t) - \ell\delta R(t+\ell), \end{aligned} \tag{7}$$

in which $t = t_n$. It is easy to show that the Taylor series expansions of the functions in (7) about t lead to

$$\begin{aligned} L_S &= \left[\tfrac{1}{2} S'' + (\mu + \beta I) S'\right] \ell^2 + O(\ell^3) \text{ as } \ell \to 0, \\ L_I &= \left[\tfrac{1}{2} I'' + (\mu + \alpha) I' - \beta S' I\right] \; \ell^2 + O(\ell^3) \text{ as } \ell \to 0, \\ L_R &= \left[\tfrac{1}{2} R'' + (\mu + \delta) R' - [(1-\sigma)\beta C - \alpha] I'\right] \ell^2 + O(\ell^3) \text{ as } \ell \to 0, \\ L_C &= \left[\tfrac{1}{2} C'' + \beta I' C + \beta I C' + (\mu + \gamma) C' - \delta R'\right] \ell^2 + O(\ell^3) \text{ as } \ell \to 0. \end{aligned} \tag{8}$$

It is evident from (8) that the principle part of the local truncations error associated with the DSS1 method is of order ℓ^2, thereby making the DSS1 method first-order accurate. The convergence and stability properties of DSS1 method will be compared with those of well-known method in the literature.

4 Numerical Simulations

4.1 Effect of time-step (ℓ)

To test the behavior of the DSS1 method, it was used to solve the *SIRC* model (1) with the parameters in Table 1 and initial values were used:$S(0) = 0.15$, $I(0) = 10^{-3}$, $C(0) = 0.44$, $R(0) = 1 - S(0) - I(0) - C(0)$.The results are compared with those obtained using the standard explicit Runge-Kutta method of order four (RK4).

The effect of time-step was monitored by using various values of time step, ℓ, in the simulations, and the results are tabulated in Table 2. It is evident from Table 1 that the DSS1 method is far more competitive (in terms of numerical stability) than the RK4 method which fails for $\ell \geq 0.0378$. Further numerous simulations suggest that, irrespective of the time step and parameter values used, the DSS1 method always gives monotonically-convergent results to the correct steady-state solutions suggesting that the method is unconditionally-convergent. The superior stability property of the novel method is consistent with the known fact that implicit methods, unlike explicit methods, are more suited for integrating nonlinear IVPs.

4.2 The effects of seasonality

In this section, the seasonal SIRC model is studied by adding a forcing term $\beta(t) = \beta_0(1 + \varepsilon\cos 2\pi t)$to system (1). The two parameters β_0 and$0 \leq \varepsilon \leq 1$ represent the rate of transmission and the degree of seasonality, respectively. The model will be considered with $\beta = 1200$ for different values of ε; $\varepsilon = 0.005$, $\varepsilon = 0.07$ and $\varepsilon = 0.3$. For all parameter values chosen, the model is run for 250 years and show the results for the last 10 years (Fig. 2(a)–(b)) and 20 years (Fig. 2(c)). The period-doubling sequence of the seasonal *SIRC* model generated by the DSS1 method is shown in Fig. 2(a)–(c). As c increases, the solution passes from a period-one-year cycle (Fig. 2(a)) to a two-year cycle (Fig. 2(b)) and to chaotic behavior (Fig. 2(c)). The behavior-solutions appear to be almost coincident with Casagrandi et al. [3], showing that the DSS1 method gives a reliable representation of the numerical solutions associated with system (1) when $\beta(t) = \beta_0(1 + \varepsilon\cos 2\pi t)$.

ℓ	0.005	0.03	1	10	1000
Method GSS1	convergence	convergence	convergence	convergence	convergence
RK4	convergence	convergence	divergence	divergence	divergence

Table 2: Effect of time-step ℓ on the convergent of the methods

5 Conclusions

A competitive finite-difference method has been developed and used for the solution of a mathematical model associated with the transmission of influenza A. Unlike the RK4 which fails when certain time-steps are used, the implicitly-derived explicit method gives results that converged (monotonically) to the true steady-states

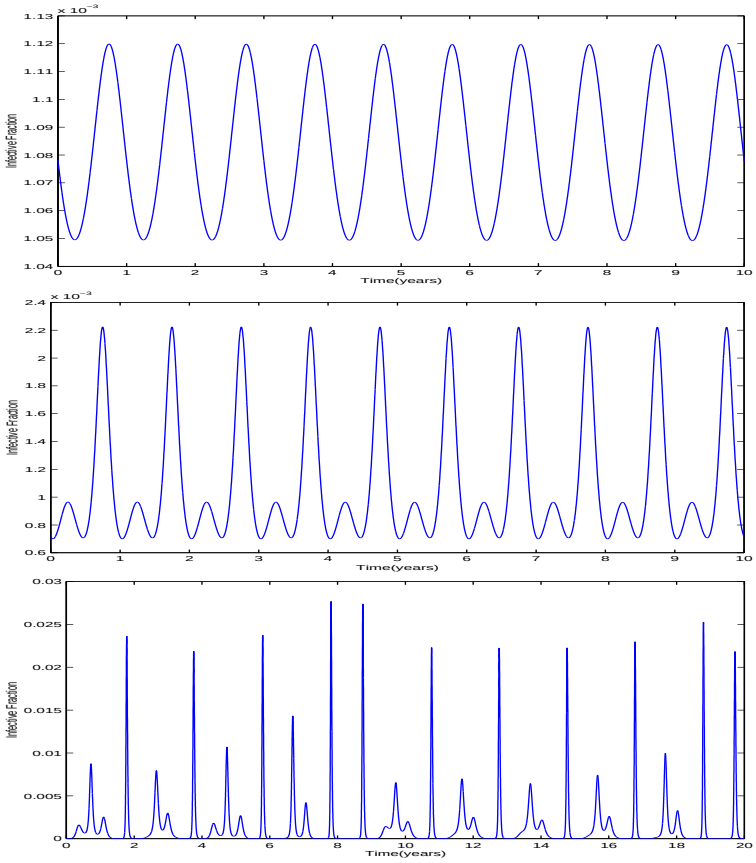

Figure 1: Time series of infective fraction using the DSS1 method with $\ell = 0.001$, $\beta = 1200$; (a) $\varepsilon = 0.005$, (b) $\varepsilon = 0.07$ and (c) $\varepsilon = 0.3$.

for any time-step used. The proposed method produced numerically-stable solutions for the *SIRC* model and also produced solutions to the seasonal *SIRC* model which were similar to reported in Casagrandi et al. [3].

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