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A non-standard finite-difference (NSFD) scheme for simultaneous infection model

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Abstract

A continuous-time differential equation model for the transmission dynamics of two different strains, with possibility of simultaneous infection, for arbitrary incurable disease(s) is formulated. A non-standard finite-difference (NSFD) scheme is constructed based on Mickens' discretization framework and analysed. The basic features of the discrete model such as positivity of solutions, the dissipativity of the system and conservation law are shown. Numerical simulations using the NSFD method confirm these results, while the standard numerical integrators (such as Euler and Runge-Kutta methods) perform poorly: they exhibit some numerical instabilities and spurious behaviour.

Keywords: Simultaneous infection; reproduction number; numerical instabilities; non-standard finite difference scheme.

1 Introduction

A number of mathematical models have been developed to explore theoretical aspects of the transmission dynamics for superinfection (strains never co-exist in a host) [6, 13, 20] and for co-infection (strains can co-exist in the host) [1, 2, 7, 15, 19, 22, 24, 26, 27]. Most of the co-infection models, for simplicity, do not allow simultaneous infection (that is, more than one parasite to be transmitted upon a single infection event [1]). Owing to the growing empirical evidence of simultaneous infection (see, for example, [5, 9, 12, 14]), which is now a major public health concern [5] and affects the epidemiology [23] and evolution [21] of infectious diseases, Zhang et al. [26, 27, 28] recently developed models which include simultaneous infection. These models are only suitable to completely curable diseases such as influenza. Alizon [1] studied the effect of co-transmission on virulence evolution in a case where parasites compete for host resources.

In this study, we begin by developing a continuous model for two incurable parasite strains (e.g., HIV strains), which can simultaneously transmit from person-to-person. Unlike [1, 26], frequency-dependent (standard) incidence, not mass action, is used which is more realistic for sexually transmitted disease like HIV. In [1, 26, 28], births and deaths are assumed, for simplicity, to occur at the same rate so that the total population size remains constant, while we allow variation of the total population size. Whilst Zhang et al. [27] restricted the transmissibility of single and double infection from the co-infected individual compared to that of single infected person, we do not. Further, we introduce a parameter θ_i, $i = 1, 2$, capturing the relative infectiousness of singly-infected individuals compared to wholly-susceptible individuals.

Since the system of the differential equations involved cannot be completely solved explicitly by analytic techniques, it is essential and vital to design reliable numerical schemes that capture the complicated dynamics of the underlying epidemiological phenomenon. It is well-known that classical methods such as Euler and Runge-Kutta method do not serve the purpose. In this

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paper, we apply the Non-Standard Finite Difference (NSFD) approach, initiated by Mickens about 3 decades ago, due to its potential effectiveness and reliability in epidemiology (see, for instance, [3, 4, 10] and the references therein). The construction of our NSFD scheme is based on an innovative way of implementing two of Mickens' rules on nonlocal approximation of nonlinear terms and complex denominator function of discrete derivatives [16, 17, 18]. Our NSFD scheme works well and shows to be free of any numerical instabilities and imposition of unduly small step size. To the best of the authors' knowledge, NSFD schemes have not been studied or designed for simultaneous infection models.

The rest of this paper is organized as follows: Section 2 presents the continuous-time model. We construct a NSFD scheme for the continuous-time model and analyse it in Section 3; we give numerical simulations, in Section 4, in order to confirm the superiority of the NSFD approach over the standard schemes.

2 Model formulation

The total human population at time t, denoted by $N(t)$, is sub-divided into four mutually-exclusive compartments of susceptible ($S(t)$), strain 1 alone infected individuals ($I_1(t)$), strain 2 alone infected individuals ($I_2(t)$) and individuals dually-infected with both strains 1 and 2 ($I_{12}(t)$), so that

$$N(t) = S(t) + I_1(t) + I_2(t) + I_{12}(t).$$

The continues-time model is given by the following deterministic system of nonlinear differential equations (a flow diagram of the model is depicted in Figure 1, and the associated variables and parameters are tabulated in Table 2:

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - (\lambda_1 + \lambda_2 + \lambda_{12})S - \mu S,\\
\frac{dI_1}{dt} &= \lambda_1 S - \theta_2\lambda_2 I_1 - (\mu + \delta_1)I_1,\\
\frac{dI_2}{dt} &= \lambda_2 S - \theta_1\lambda_1 I_2 - (\mu + \delta_2)I_2,\\
\frac{dI_{12}}{dt} &= \lambda_{12} S + \theta_2\lambda_2 I_1 + \theta_1\lambda_1 I_2 - (\mu + \delta_{12})I_{12},
\end{aligned} \tag{1}$$

In addition to co-infection, the aforementioned model (1) allows concurrent infection of the two strains which makes the model complicated. Traditionally, it has been assumed in two or more strains modelling (e.g., [2, 7, 15, 19, 22, 24]) that co-transmission is not allowed. One of the technical problems with the model (1) is that the interior equilibrium cannot be explicitly written. Furthermore, it is easy to show that, using next generation method [25], the associated *basic reproduction number* of the model (1), denoted by $\mathcal{R}_0$, is given by

$$\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_{12}\}$$

where, $\mathcal{R}_1 = \frac{\beta_1}{K_1}$, $\mathcal{R}_2 = \frac{\beta_2}{K_2}$ and $\mathcal{R}_{12} = \frac{\beta_{12}}{K_3}$. It is clear that each threshold quantity $\mathcal{R}_1$, $\mathcal{R}_2$ and $\mathcal{R}_{12}$ presents the *basic reproduction number* associated with the infectious class I_1, I_2 and I_{12}, respectively and can be seen as the product of the infection rates and the average duration of infectivity in each case. The *basic reproduction number* of the model (1) is indeed the number of secondary infections (either single-infections or concurrent infections) that one dually-infected individual with strain 1 and 2 will produce in an entirely susceptible population during its lifespan as infectious. This reproduction number depends on the interaction between the two diseases which includes simultaneous infection effects.

Variable	**Interpretation**
S	Population of susceptible individuals
I_1	Population of infected individuals with strain 1 only
I_2	Population of infected individuals with strain 2 only
I_{12}	Population of dually-infected individuals with both strains
λ_1	Strain 1 force of infection
λ_2	Strain 2 force of infection
λ_{12}	Simultaneous force of infection
Parameter	**Interpretation**
Π	Recruitment rate
μ	Natural death rate
β_1	Transmission rate of strain 1
β_2	Transmission rate of strain 2
β_{12}	Transmission rate of simultaneous infection of strain 1 and 2
θ_i, $i = 1, 2$	Modification parameter for relative infectiousness of singly-infected individuals in comparison to wholly-susceptible individuals
η	Modification parameter for relative infectiousness of dually-infected individuals in comparison to mono-infected individuals
δ_1	Strain 1 induced death rate for individuals
δ_2	Strain 2 induced death rate for individuals
δ_{12}	Rate of mortality due to dual infection

Table 1: **Description of the variables and parameters model** (1).

3 Non-standard finite difference (NSFD) method

Adding all the equations in model (1) gives

$$\frac{dN}{dt} = \Pi - \mu N - \delta_1 I_1 - \delta_2 I_2 - \delta_{12} I_{12}.$$

Thus, we have

$$\frac{dN}{dt} \leq \Pi - \mu N,$$

which, following the terminology in [17], is a conservation law. The exact scheme of this conservation law is

$$\frac{N^{n+1} - N^n}{\phi(\Delta t)} \leq \Pi - \mu N^{n+1}, \tag{2}$$

where $\phi = \phi(\Delta t) = \frac{e^{\mu \Delta t} - 1}{\mu}$ is the denominator function of the discrete derivative, such that

$$\phi(h) = h + \mathcal{O}(h^2), \text{ where } h = \Delta t.$$

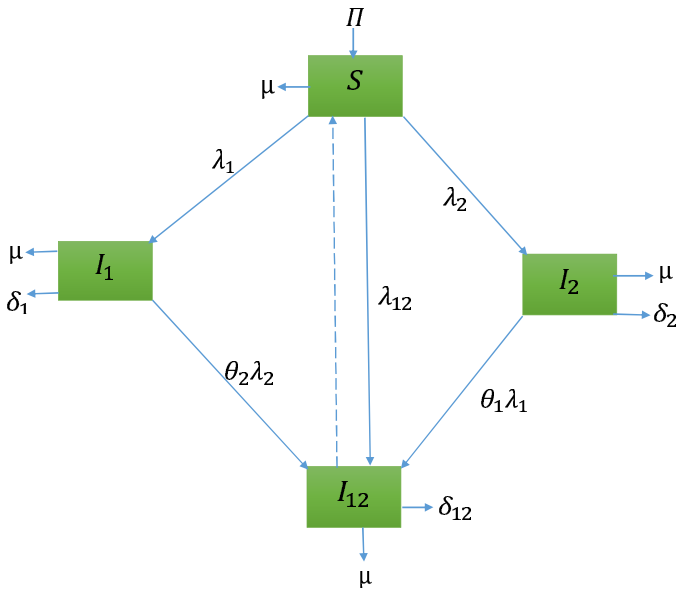

Figure 1: Schematic diagram of the model (1). Solid arrows indicate transitions and dashed arrow indicates interaction. Expressions next to arrows show the *per capita* flow rate between compartments.

Given $(S^n, I_1^n, I_2^n, I_{12}^n) \in \Omega$ and $\tilde{N}^n = I_1^n + I_2^n + I_{12}^n$, the NSFD scheme for the model (1) is as follows:

$$\begin{aligned}
\frac{S^{n+1}-S^n}{\phi(h)} &= \Pi - \left(\frac{\beta_1(I_1^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} + \frac{\beta_2(I_2^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} + \frac{\beta_{12} I_{12}^n}{S^{n+1}+\tilde{N}^n}\right) S^{n+1} \\
&\quad - \mu S^{n+1}, \\
\frac{I_1^{n+1}-I_1^n}{\phi(h)} &= \frac{\beta_1(I_1^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} S^{n+1} - \frac{\beta_2\theta_2(I_2^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} I_1^{n+1} - (\mu+\delta_1) I_1^{n+1}, \\
\frac{I_2^{n+1}-I_2^n}{\phi(h)} &= \frac{\beta_2(I_2^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} S^{n+1} - \frac{\beta_1\theta_1(I_1^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} I_2^{n+1} - (\mu+\delta_2) I_2^{n+1}, \\
\frac{I_{12}^{n+1}-I_{12}^n}{\phi(h)} &= \frac{\beta_{12} I_{12}^n}{S^{n+1}+\tilde{N}^n} S^{n+1} + \frac{\beta_2\theta_2(I_2^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} I_1^{n+1} + \frac{\beta_1\theta_1(I_1^n+\eta I_{12}^n)}{S^{n+1}+\tilde{N}^n} I_2^{n+1} \\
&\quad - (\mu+\delta_{12}) I_{12}^{n+1}.
\end{aligned} \tag{3}$$

The NSFD scheme (3) is fundamentally different from the two strain discrete model proposed in [8, 11]. Whilst the scheme (3) includes both co-infection and simultaneous infection, these references do not.

3.1 Basic qualitative properties of the NSFD scheme

Theorem 3.1 *The NSFD scheme* (3) *defines a discrete dynamical system on the region* Ω.

Proof. Let $S^n \geq 0$, $I_1^n \geq 0$, $I_2^n \geq 0$ and $I_{12}^n \geq 0$, then the first equation in the system (3) is equivalent to the following quadratic equation in S^{n+1}:

$$a[S^{(n+1)}]^2 + bS^{n+1} + c = 0, \tag{4}$$

where,

$$a = 1 + \phi\mu,$$
$$b = -(S^n + \Pi\phi) + (1 + \mu\phi)\tilde{N}^n + \phi\beta_1(I_1^n + \eta I_{12}^n) + \phi\beta_2(I_2^n + \eta I_{12}^n) + \phi\beta_{12}I_{12}^n,$$
$$c = -(S^n + \Pi\phi)\tilde{N}^n.$$

The unique positive root of (4) is given by

$$S^{n+1} = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \tag{5}$$

Using this positive solution of S^{n+1}, we solve the system (3) for I_1^{n+1}, I_2^{n+1} and I_{12}^{n+1} in a sequential way to obtain the following:

$$\begin{aligned}
I_1^{n+1} &= \frac{(S^{n+1} + \tilde{N}^n)I_1^n + \phi\beta_1(I_1^n + \eta I_{12}^n)S^{n+1}}{[1 + \phi(\mu + \delta_1)](S^{n+1} + \tilde{N}^n) + \beta_2\theta_2(I_2^n + \eta I_{12}^n)}, \\
I_2^{n+1} &= \frac{(S^{n+1} + \tilde{N}^n)I_2^n + \phi\beta_2(I_2^n + \eta I_{12}^n)S^{n+1}}{[1 + \phi(\mu + \delta_2)](S^{n+1} + \tilde{N}^n) + \beta_1\theta_1(I_1^n + \eta I_{12}^n)}, \\
I_{12}^{n+1} &= \frac{1}{[1 + \phi(\mu + \delta_{12})]}\left[I_{12}^n + \frac{\phi}{S^{n+1} + \tilde{N}^n}\left(\beta_{12}I_{12}^n S^{n+1} + \beta_2\theta_2(I_2^n + \eta I_{12}^n)I_1^{n+1}\right.\right. \\
&\quad \left.\left. + \beta_1\theta_1(I_1^n + \eta I_{12}^n)I_2^{n+1}\right)\right].
\end{aligned} \tag{6}$$

This shows that the solution sequence S^{n+1}, I_1^{n+1}, I_2^{n+1} and I_{12}^{n+1} exists and it is unique. It is clear from the induction and the discrete system (6) that $S^{n+1} \geq 0$, $I_1^{n+1} \geq 0$, $I_2^{n+1} \geq 0$ and $I_{12}^{n+1} \geq 0$. Hence, the NSFD method shows positivity of solutions for all positive initial data. In order to show that the NSFD scheme (3) preserves the upper bound property in the definition of Ω, we consider equivalent of (2) given by

$$N^{n+1} \leq \frac{N^n}{1 + \mu\phi} + \frac{\Pi\phi}{1 + \mu\phi} \tag{7}$$

By using the discrete Gronwall inequality from the right and the left sides, we obtain

$$N^n \leq \frac{\Pi}{\mu} + (N_0 - \frac{\Pi}{\mu})(1 + \mu\phi)^{-n} \tag{8}$$

This leads to

$$0 \leq N^n \leq \frac{\Pi}{\mu} \text{ if } 0 \leq N_0 \leq \frac{\Pi}{\mu}.$$

3.1.1 Stability of the discrete model equilibria

Lemma 3.1 *The NSFD scheme* (3) *has no ghost or spurious equilibria.*

Proof. Let $\hat{\mathcal{E}} = \left(\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_{12}\right)$ be a fixed-point of (3), then

$$\begin{aligned}
0 &= \Pi - \left(\frac{\beta_1(\hat{I}_1 + \eta\hat{I}_{12})}{\hat{S}+\hat{N}} + \frac{\beta_2(\hat{I}_2 + \eta\hat{I}_{12})}{\hat{N}} + \frac{\beta_{12}\hat{I}_{12}}{\hat{N}}\right) - \mu\hat{S},\\
0 &= \frac{\beta_1(\hat{I}_1 + \eta\hat{I}_{12})}{\hat{N}}\hat{S} - \frac{\beta_2\theta_2(\hat{I}_2 + \eta\hat{I}_{12})}{\hat{N}}\hat{I}_1 - (\mu+\delta_1)\hat{I}_1,\\
0 &= \frac{\beta_2(\hat{I}_2 + \eta\hat{I}_{12})}{\hat{N}}\hat{S} - \frac{\beta_1\theta_1(\hat{I}_1 + \eta\hat{I}_{12})}{\hat{N}}\hat{I}_2 - (\mu+\delta_2)\hat{I}_2,\\
0 &= \frac{\beta_{12}\hat{I}_{12}}{\hat{N}}\hat{S} + \frac{\beta_2\theta_2(\hat{I}_2 + \eta\hat{I}_{12})}{\hat{N}}\hat{I}_1 + \frac{\beta_1\theta_1(\hat{I}_1 + \eta\hat{I}_{12})}{\hat{N}}\hat{I}_2 - (\mu+\delta_{12})\hat{I}_{12},
\end{aligned} \tag{9}$$

The system (9) is equivalent the continuous system (1) at a steady-state. Thus, it is follows that the fixed points of the NSFD scheme (9) correspond to that of the continuous system (1). Hence the prove is complete.

Theorem 3.2 *If $\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_{12}\} < 1$, the disease-free fixed point, $\mathcal{E}_0$, of NSFD scheme* (3) *is locally asymptotically stable and unstable if $\mathcal{R}_0 > 1$.*

Proof.
The Jacobian matrix, at $\mathcal{E}_0$, of the system (3) is

$$J(\mathcal{E}_0) = \begin{bmatrix}
(\mu\,\phi+1)^{-1} & -\frac{\phi\,\beta_1}{\mu\,\phi+1} & -\frac{\phi\,\beta_2}{\mu\,\phi+1} & -\frac{\phi\,[(\beta_1+\beta_2)\eta+\beta_{12}]}{\mu\,\phi+1}\\
0 & \frac{\phi\,\beta_1+1}{1+\phi\,(\mu+\delta_1)} & 0 & \frac{\phi\,\beta_1\eta}{1+\phi\,(\mu+\delta_1)}\\
0 & 0 & \frac{\phi\,\beta_2+1}{1+\phi\,(\mu+\delta_2)} & \frac{\phi\,\beta_2\eta}{1+\phi\,(\mu+\delta_2)}\\
0 & 0 & 0 & \frac{\phi\,\beta_{12}+1}{1+\phi\,(\mu+\delta_{12})}
\end{bmatrix}$$

and has the following eigenvalues: $r_1 = \frac{1}{1+\mu\phi}$, $r_2 = \frac{\phi\mathcal{R}_1+1/K_1}{\phi+1/K_1}$, $r_3 = \frac{\phi\mathcal{R}_2+1/K_2}{\phi+1/K_2}$ and $r_4 = \frac{\phi\mathcal{R}_{12}+1/K_3}{\phi+1/K_3}$. It follows that $|r_1| < 1$ and $|r_i| < 1$ for $i = 2, 3, 4$ if and only if $\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_{12}\} < 1$.

Theorem 3.3 *Assume that $\mathcal{R}_0 < 1$. Then the disease-free fixed point, $\mathcal{E}_0$, of NSFD scheme* (3) *is globally asymptotically stable.*

Proof.
The sequence $(S^n, I_1^n, I_2^n, I_{12}^n)_{n\geq 0}$ in $\Omega \subset \mathbb{R}_+^4$ being bounded, it follows from Bolzano–Weierstrass theorem, that there exits a subsequence $(S^{n_k}, I_1^{n_k}, I_2^{n_k}, I_{12}^{n_k})$ of $(S^n, I_1^n, I_2^n, I_{12}^n)$ that is convergent. Denote by $(S^*, I_1^*, I_2^*, I_{12}^*)$ the limit of $(S^{n_k}, I_1^{n_k}, I_2^{n_k}, I_{12}^{n_k})$ as $k \to +\infty$. Replace n by n_k in (5) and (6) and let $k \to +\infty$. In view of the condition $\mathcal{R}_0 < 1$, we necessarily have $(S^*, I_1^*, I_2^*, I_{12}^*) = \mathcal{E}_0$. Since $\mathcal{E}_0$ is LAS by Theorem 3.2, there exists $\delta > 0$ such that $\lim_{n\to\infty}(S^n, I_1^n, I_2^n, I_{12}^n) = \mathcal{E}_0$ whenever $\| (S^0, I_1^0, I_2^0, I_{12}^0) - \mathcal{E}_0 \| \leq \delta$. From the convergence of $(S^{n_k}, I_1^{n_k}, I_2^{n_k}, I_{12}^{n_k})$ to $\mathcal{E}_0$, there exists an integer k_0 such that $\| (S^{n_k}, I_1^{n_k}, I_2^{n_k}, I_{12}^{n_k}) - \mathcal{E}_0 \| \leq \delta$ whenever $k \geq k_0$. Then

$$\lim_{n\to\infty}(S^n, I_1^n, I_2^n, I_{12}^n) = \lim_{n\geq n_{k_0}}(S^n, I_1^n, I_2^n, I_{12}^n) = \mathcal{E}_0.$$

4 Numerical simulations

To illustrate the dynamically consistent behaviour, which includes the positivity of solutions, stability and attractiveness properties, of the NSFD method, comparisons are made with RK4

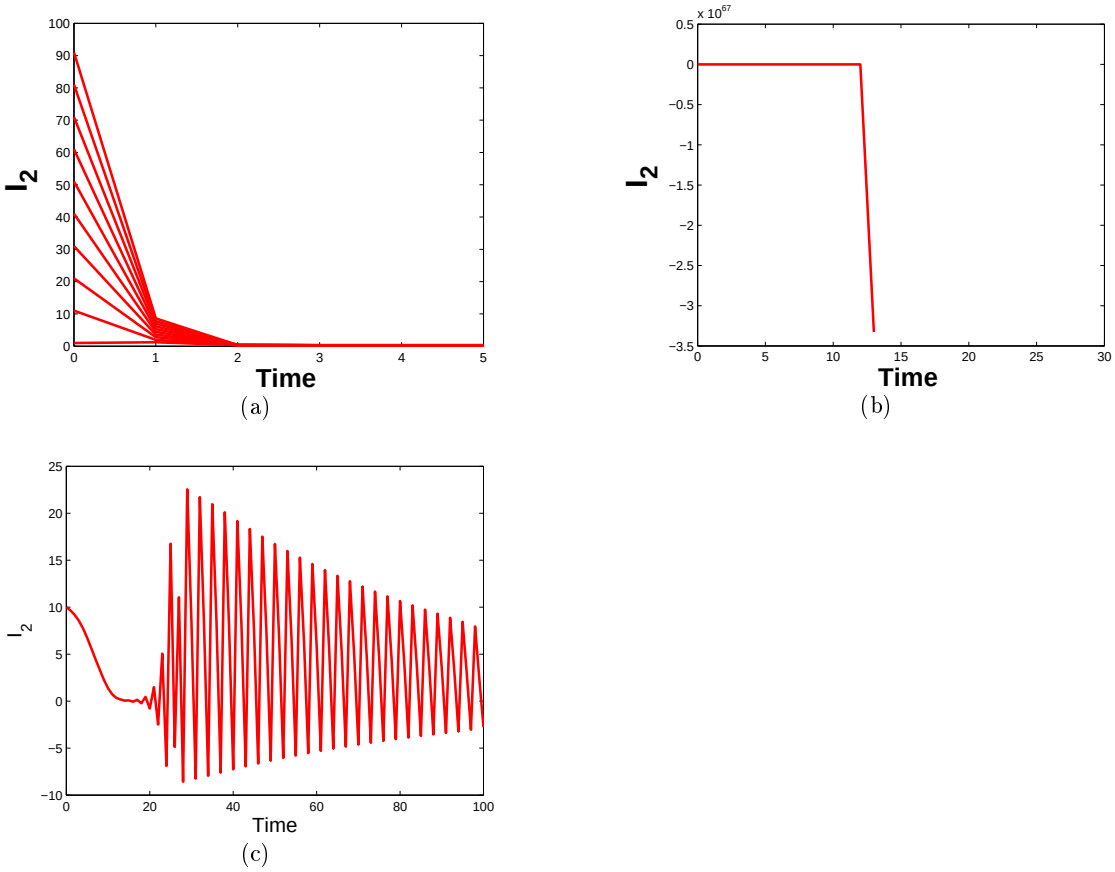

Figure 2: Solution profile of I_1 generated using (2(a)) NSFD method ($h = 1000$) (2(b)) RK4 ($h = 0.04$) and (2(c)) Euler ($h = 0.02$).

and Euler methods. First, simulations are carried out using the following set of parameter values: $\mu = 1/50$, $\beta_1 = 0.7$, $\beta_2 = 0.7$, $\beta_3 = 0.8$, $\Pi = 2$, $\delta_1 = 0.7$, $\delta_2 = 0.7$, $\delta_3 = 0.8$, $\eta = 20$, $\theta_2 = 10$ and $\theta_1 = 10$, to test the positivity property of the model (3) (guaranteed by Theorem 3.1). The results obtained (see Figure 2) show that the solution profiles of I_2 generated by the NSFD scheme faithfully preserve the property of positivity of the solutions (despite a relative large step-size is used) while both RK4 and Euler, with small step-sizes, fail by producing negative solutions which do not make sense in biology.

Using the same set of parameter values as above, Figure 3(a) shows that the NSFD method satisfies the conservation law (given by equation (2)). Thus, the NSFD always displays solutions which do not exceed the maximum total population value Π/μ. The standard numerical methods under consideration (i.e., RK4 and Euler) fail to capture this important property (Figures 3(b) and 3(c)).

5 Conclusion

A continuous-time susceptible infected (SI) model for the simultaneous infection involving two strains is designed and used to construct its discrete equivalence. The basic features of the discrete model such as positivity of solutions, the dissipativity of the system and conservation law are shown. Furthermore, the disease-free fixed point is shown to be globally asymptotically stable. Numerical simulations using the NSFD method confirm the basic properties of the discrete model, while the standard numerical integrators (such as Euler and Runge-Kutta methods) perform poorly: they exhibit some numerical instabilities and spurious behaviour.

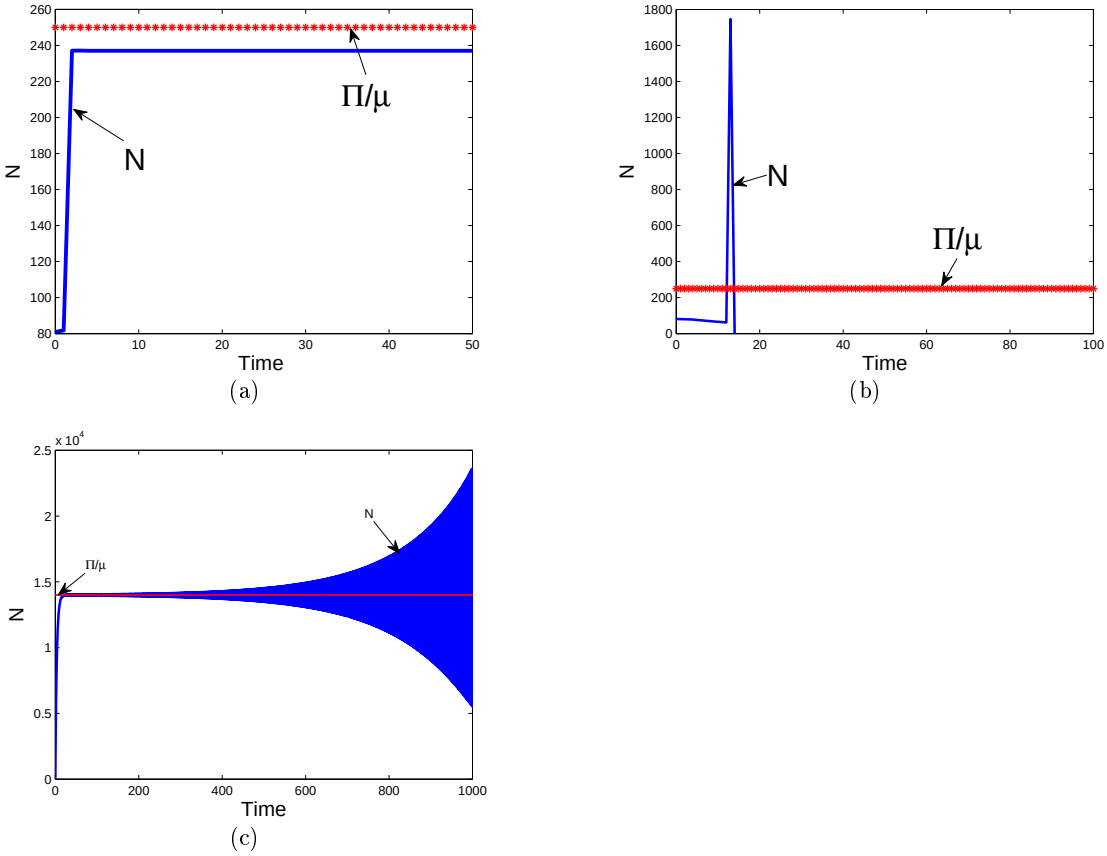

Figure 3: Solution profile of N generated using (2(a)) NSFD method ($h = 1000$) (2(b)) RK4 ($h = 0.04$) and (2(c)) Euler ($h = 0.025$).

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