# Positivity-preserving nonstandard finite difference schemes for cross-diffusion equations in biosciences

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**Abstract**

We design nonstandard finite difference (NSFD) schemes which are unconditionally dynamically consistent with respect to the positivity property of solutions of cross-diffusion equations in biosciences. This settles a problem that was open for quite some time. The study is done in the setting of three concrete and highly relevant cross-diffusion systems regarding tumor growth, convective predator-prey pursuit and evasion model and reaction-diffusion-chemotaxis model. It is shown that NSFD schemes used for classical reaction-diffusion equations, such as the Fisher equation, for which the solutions enjoy the positivity property, are not appropriate for cross-diffusion systems. The reliable NSFD schemes are therefore obtained by considering a suitable implementation on the cross-diffusive term of Mickens' rule of nonlocal approximation of nonlinear terms, apart from his rule of complex denominator function of discrete derivatives. We provide numerical experiments that support the theory as well as the power of the NSFD schemes over the standard ones. In the case of the cancer growth model, we demonstrate computationally that our NSFD schemes replicate the property of traveling wave solutions of developing shocks observed in [14].

**AMS Subject Classification (2010):** 65L12; 65L99; 65M06; 65M99; 92D30.

**Keywords:** nonstandard finite difference method, dynamical consistency, cross-diffusion equations, reaction-diffusion-chemotaxis equations, tumor growth, predator-prey pursuit and evasion model.

## 1 Introduction

Diffusion equations have been extensively studied for the modeling of biological processes such as animal dispersal, spread of diseases and biofilm growth. Often, the models are in the form of reaction-diffusion and advection-reaction-diffusion equations [13, 18, 19, 23]. In contrast, the mathematical analysis for cross-diffusion equations is a challenge which is largely undeveloped. A cross-diffusion system is characterized by the fact that the diffusion matrix is not strictly diagonal and even not symmetric positive. Thus, in the equation for one species, there is at least one diffusion-type term that involves another species. In Murray's mathematical biology book [18, 19], which is a good attempt to cover the many topics in biosciences, some cross-diffusion equations of interest in applications have been identified. Furthermore, cross-diffusion equations are at the core of modeling of several natural processes such as cancer growth [3, 9], population dynamics via, for instance, Volterra-Lotka cross-diffusion systems [7, 12, 22] and chemotaxis [11].

From a theoretical point of view, cross-diffusion equations are challenging mainly because they are strongly coupled nonlinear parabolic systems, which do not enjoy the maximum principle and thus deriving a priori estimates and proving the existence of positive solutions is not easy. Nevertheless, some results on global and local existence of solutions as well as on their long-time behavior have been established in [7, 12]. Equally, the design, for cross-diffusion equations, of reliable numerical methods that produce

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positive solutions has been an open problem for many years now [17]. The current paper deals precisely with this outstanding problem in the following three settings: a model for cancer growth [14], a convective predator-prey pursuit and evasion model [19] and the basic reaction-diffusion-chemotaxis model [19].

We use the nonstandard finite difference (NSFD) approach. In the first step, we use a boundedness and positivity-preserving NSFD scheme that we introduced in [2] for classical diffusion equations, including the Fisher equation. This scheme was constructed by coupling Mickens' rules (of complex denominator functions of discrete derivatives and nonlocal approximation of nonlinear terms) with a suitable functional relation between the time and the space step sizes. Unfortunately, when applied to cross-diffusion equations, the resulting NSFD schemes are not dynamically reliable. In the second step, we consider an alternative strategy, which apart from Mickens' rule on the denominator, consists in using a special nonlocal approximation of the cross-diffusion terms with the step sizes varying independently from one another. We then obtain NSFD schemes which are unconditionally dynamically consistent with respect to the positivity property of the solutions of cross-diffusion equations.

Our results, which were announced in [5], are mostly elaborated for the cancer growth model because the initial motivation of this paper was to provide positive NSFD solutions for this model. The rest of the paper is organized as follows. In the next section, we present a cancer growth model and design several NSFD schemes for it. Sections 3 and 4 deal with the convective predator-prey pursuit and evasion model and the basic reaction-diffusion-chemotaxis model, respectively. Numerical experiments that support the reliability of our NSFD schemes are provided in each section. The last section is devoted to concluding remarks.

## 2 A model of malignant invasion

In [18], it is stated that cross-diffusion does not arise in genuinely practical models. In this section, we add to the few practical examples mentioned in this reference, a cross-diffusion model that governs solid tumor growth. We consider a one-dimensional model of malignant invasion proposed in [14], where $u = u(x,t)$, $c = c(x,t)$ and $p = p(x,t)$ are concentrations of invasive cells, connective tissue and protease, respectively. The model is presented in nondimensionalized form, with $u$ scaled so that the carrying capacity is unit. In the unlikely case when connective tissues are absent, the invasive cells grow in a logistic manner:

$$\frac{du}{dt} = u(1-u). \tag{1}$$

In particular, invasive cells have an invasive flux of $u\frac{\partial c}{\partial x}$ into connective tissues, which leads to the reaction-advection equation

$$\frac{\partial u}{\partial t} = u(1-u) - \frac{\partial}{\partial x}\left(u\frac{\partial c}{\partial x}\right). \tag{2}$$

Connective tissues are dissolved by proteases in accordance with the mass action principle:

$$\frac{\partial c}{\partial t} = -pc. \tag{3}$$

The latter are produced by invasive cells upon contact with connective tissues, according to the law

$$\frac{\partial p}{\partial t} = \epsilon^{-1}(uc - p), \tag{4}$$

where the parameter $\epsilon > 0$ supposed to be small reflects the fact that the units of protease are far smaller than those of connective tissues and invading cells, and their dynamics are seen on a shorter time scale.

The dimensionless system (2)-(4) forms the so-called cross-diffusion equations because Eq (2) of invasive cells has a diffusion-type term that involves another species, namely $c$, instead of the usual diffusion term $\frac{\partial^2 u}{\partial x^2}$. Moreover, unlike classical diffusion equations, the presence of the negative sign in front of the cross-diffusive term in Eq. (2) is typical of cross-diffusion systems in biosciences and this is one of the sources of difficulties. Here, we focus on an initial value problem and thus complete the system with initial conditions

$$u(x,t) = u^0(x),\ c(x,t) = c^0(x) \text{ and } p(x,t) = p^0(x), \tag{5}$$

for $x \in \mathbb{R}$ and $t > 0$. The problem could be considered with appropriate boundary conditions [10].

By setting the right-hand side to be zero, it follows that the system (2)-(4) has three types of constant steady-state solutions $E = (u, c, p)$: the fully malignant equilibrium $E_m = (1, 0, 0)$; the normal healthy equilibrium $E_n = (0, c, 0)$, where $c > 0$ is any constant, and the trivial equilibrium $E_t = (0, 0, 0)$. By seeking traveling wave solutions, it can be shown, similarly to the Fisher-KPP equation [13, 19], that the solutions enjoy the property

$$u(x,t) \geq 0,\ c(x,t) \geq 0,\ p(x,t) \geq 0, \tag{6}$$

with $c$ decreasing in time whenever the initial conditions are nonnegative: $u^0(x) \geq 0$, $c^0(x) \geq 0$ and $p^0(x) \geq 0$. For existence of solutions for some cross-diffusion equations, we refer to [7, 12].

The main purpose of this paper is to design nonstandard finite difference (NSFD) schemes that replicate he property (6) irrespective of the values of the time and space step sizes $\Delta t$ and $\Delta x$. We denote by $u_m^k$, $c_m^k$ and $p_m^k$ the sequences in $m \in \mathbb{Z}$ and $k \in \mathbb{N}$ of approximations of $u$, $c$ and $p$ at the grid points $x_m = m\Delta x$ and $t_k = k\Delta t$.

The limit space-independent case of Eq. (2) is the logistic equation (1), which has the exact scheme [15]:

$$\frac{u^{k+1} - u^k}{\exp(\Delta t) - 1} = u^k(1 - u^{k+1}).$$

The advantage of the complex denominator function $\exp(\Delta t) - 1$, over the standard one $\Delta t$, is clear: there s no error between the continuous and discrete solutions of the initial value problem associated with (1). In what follows, we set

$$\phi(\Delta t) = \exp(\Delta t) - 1.$$

Our strategy is that all schemes designed in this work reduce to the exact scheme in the space independent equation limit case. Similarly, we make use of a function $\psi(\Delta x) \geq 0$ satisfying, like $\phi(\Delta t)$, the asymptotic elation:

$$\psi(\Delta x) = \Delta x + O[(\Delta x)^2].$$

Typically, when the stationary equation is the harmonic oscillator, the denominator function of the discrete derivative in the exact scheme is $\psi(\Delta x)^2 = 4\sin^2\left(\frac{\Delta x}{2}\right)$, [15].

Following the usual rules of the nonstandard approach, namely the nonlocal approximation of nonlinear erms and the use of complex functions as denominators of discrete derivatives [1, 15], Eq (3) and Eq (4) are readily approximated by

$$\frac{c_m^{k+1} - c_m^k}{\phi(\Delta t)} = -p_m^k c_m^{k+1} \text{ or } c_m^{k+1} = \frac{c_m^k}{1 + \phi(\Delta t) p_m^k} \tag{7}$$

and

$$\frac{p_m^{k+1} - p_m^k}{\epsilon\phi(\epsilon^{-1}\Delta t)} = \epsilon^{-1}(u_m^k c_m^{k+1} - p_m^{k+1}) \text{ or } p_m^{k+1} = \frac{p_m^k + \phi(\epsilon^{-1}\Delta t) u_m^k c_m^{k+1}}{1 + \phi(\epsilon^{-1}\Delta t)}, \tag{8}$$

respectively. Notice that to approximate $p$ in Eq (8), we use $c_m^{k+1}$ that is already computed.

The challenge is with Eq (2) where the NSFD methods used so far for standard reaction-diffusion equations are not appropriate, in view of the cross-diffusive term. To illustrate this fact, we consider the NSFD scheme

$$\frac{u_m^{k+1} - u_m^k}{\phi(\Delta t)} = u_m^k(1 - u_m^{k+1}) - \frac{u_m^k c_{m+1}^k - (u_m^k + u_{m-1}^k)c_m^k + u_{m-1}^k c_{m-1}^k}{\psi(\Delta x)^2}, \tag{9}$$

proposed in [2] and elsewhere in the literature for the Fisher-KPP equation, a classical reaction-diffusion equation, and which, on imposing the functional relation

$$\psi(\Delta x)^2 = 2\phi(\Delta t) \tag{10}$$

between the step sizes, takes the explicit form

$$u_m^{k+1} = \frac{2u_m^k[1 + \phi(\Delta t)] - [u_m^k c_{m+1}^k - (u_m^k + u_{m-1}^k)c_m^k + u_{m-1}^k c_{m-1}^k]}{2[1 + \phi(\Delta t) u_m^k]}. \tag{11}$$

From Eq (11), it is seen that the positivity of $u_m^{k+1}$ is not guaranteed. This is illustrated on Fig. 5 where, for instance, $u_2^1 < 0$ and shows the need of dealing with cross-diffusion equations differently. Despite its shortcomings, the NSFD scheme (9) is the basis for the new schemes designed below. We will design suitable corrections of scheme (9). To this end, we proceed in two different manners. Firstly, we approximate Eq (2) by

$$\frac{u_m^{k+1} - (u_m^k + u_{m-1}^k)/2}{\phi(\Delta t)} = u_m^k(1 - u_m^{k+1}) - \frac{u_m^k c_{m+1}^k - (u_m^k + u_{m-1}^k)c_m^k + u_{m-1}^k c_{m-1}^k}{\psi(\Delta x)^2}, \tag{12}$$

which, under the functional relation (10), reads

$$u_m^{k+1} = \frac{2\phi(\Delta t)u_m^k + u_m^k(1 - c_{m+1}^k) + u_{m-1}^k(1 - c_{m-1}^k) + (u_m^k + u_{m-1}^k)c_m^k}{2[1 + \phi(\Delta t)u_m^k]}. \tag{13}$$

We summarize our findings as follows:

**Theorem 1** *For $u_m^0 \geq 0, c_m^0 \geq 0$ and $p_m^0 \geq 0$, we have $c_m^k \geq 0$ and $p_m^k \geq 0$ with the sequence $\{c_m^k\}$ being decreasing in $k$. Furthermore, if $c_m^0 \leq 1$ and if the condition (10) is satisfied, then $u_m^k \geq 0$.*

Several positivity-preserving NSFD schemes have been constructed in the literature, see for example [2, 8, 15, 17]. The underlying fact in the process is that the positive and negative parts of the right hand side of the differential models are distinctly known. The negative part is then dealt with by nonlocal approximation or the use of a suitable complex denominator function. In the case of the cross-diffusion model under consideration, this distinction is not clear. The main trick in the second discretization of Eq (2) is to decompose the approximation of the cross-diffusive term $\frac{\partial}{\partial x}\left(u\frac{\partial c}{\partial x}\right)$ in Eq. (9) into its positive and negative parts. The negative part is then multiplied by $2u_m^{k+1}/(u_m^{k+1} + u_m^k)$, which approximates the constant 1 as $\Delta t \to 0$. We then obtain the NSFD scheme

$$\frac{u_m^{k+1} - u_m^k}{\phi(\Delta t)} = u_m^k(1 - u_m^{k+1}) + \frac{(u_m^k + u_{m-1}^k)c_m^k}{\psi(\Delta x)^2} - \frac{u_m^k c_{m+1}^k + u_{m-1}^k c_{m-1}^k}{\psi(\Delta x)^2} \times \frac{2u_m^{k+1}}{u_m^{k+1} + u_m^k}, \tag{14}$$

which corresponds to the following quadratic equation in $u_m^{k+1}$:

$$A_m^k (u_m^{k+1})^2 + B_m^k u_m^{k+1} + D_m^k = 0,$$

where

$$\begin{aligned} A_m^k &= 1 + \phi(\Delta t)u_m^k, \\ B_m^k &= -\phi(\Delta t)u_m^k - R(u_m^k + u_{m-1}^k)c_m^k + 2R(u_m^k c_{m+1}^k + u_{m-1}^k c_{m-1}^k), \\ D_m^k &= -(u_m^k)^2 - R(u_m^k + u_{m-1}^k)u_m^k c_m^k. \end{aligned} \tag{15}$$

When $u_m^k \geq 0$ and $c_m^k \geq 0$ so that $A_m^k \geq 0$ and $D_m^k \leq 0$, the only nonnegative root of the quadratic equation is

$$u_m^{k+1} = \frac{-B_m^k + \sqrt{(B_m^k)^2 - 4A_m^k D_m^k}}{2A_m^k}. \tag{16}$$

An alternative NSFD scheme to (14) is obtained by using $u_m^{k+1}/u_m^k \approx 1$, an idea that is exploited in [8] for productive-destructive systems where the positive (productive) and negative (destructive) terms of the model are, as mentioned above, unequivocally known. This leads to the NSFD scheme

$$\frac{u_m^{k+1} - u_m^k}{\phi(\Delta t)} = u_m^k(1 - u_m^{k+1}) + \frac{(u_m^k + u_{m-1}^k)c_m^k}{\psi(\Delta x)^2} - \frac{u_m^k c_{m+1}^k + u_{m-1}^k c_{m-1}^k}{\psi(\Delta x)^2} \times \frac{u_m^{k+1}}{u_m^k}, \tag{17}$$

which, on setting

$$R = \frac{\phi(\Delta t)}{\psi(\Delta x)^2}, \tag{18}$$

is equivalent to

$$u_m^{k+1} = \frac{(1 + \phi(\Delta t))u_m^k + R(u_m^k + u_{m-1}^k)c_m^k}{1 + \phi(\Delta t)u_m^k + R(u_m^k c_{m+1}^k + u_{m-1}^k c_{m-1}^k)/u_m^k}. \tag{19}$$

We have established the following result:

**Theorem 2** *The NSFD schemes (16) and (19) are unconditionally dynamically consistent with respect to positivity.*

**Remark 3** *A few more comments are in order for the NSFD schemes (13), (16) and (19). They have no spurious fixed-points as they preserve the equilibria of the continuous model (2)-(4). A comment on the stability will be made later when we deal with traveling wave solutions. In the case when* $u_m^k = 0$*, the scheme (13) and (16) will be preferred to the scheme (19). The latter scheme can still be used provided that an appropriate limit is taken to deal with the indetermination* $0/0$*. Note that the scheme* (16) *is also suitable when dealing with reaction terms that are fractions of the dependent variable such as the Holling function of types II and III, [6].*

**Remark 4** *While there is actually no need for all three NSFD schemes, each is, however, a valid scheme in its own and of themselves. Nevertheless, we opted to display the three schemes for the purposes of completeness, specifically that concerns on systematic methodologies of constructing NSFD schemes are often raised in the literature. All these schemes are qualitatively and dynamically the same in sense that they preserve positivity of the solution in such a way that we have the increase of the connective tissue, the decrease of the invasive cells and the growth of protease. The natural way in which the complex denominator function* $\phi(\Delta t)$ *comes in and its relevance, which were mentioned earlier, are inherent to exact schemes that have been designed for a wide range of differential models, [21, 15, 17]. For general NSFD schemes [1, 15, 17], the role of the complex denominator function and of the nonlocal approximation is to incorporate the main feature (e.g., eigenvalues of the Jacobian matrix at equilibria), of the continuous system into the numerical method in order for the latter to be dynamically consistent for any value of the step size.*

Theorem 1 and Theorem 2 are illustrated in Figs. 1 – 3 where we took $\epsilon = 0.2$ and $\Delta t = 1.0$. Motivated by [4, 10], we use the following initial conditions:

$$u^0(x) = \exp(-x^2);\ c^0(x) = 1 - 0.5u^0(x) \text{ and } p^0(x) = 0.5u^0(x).$$

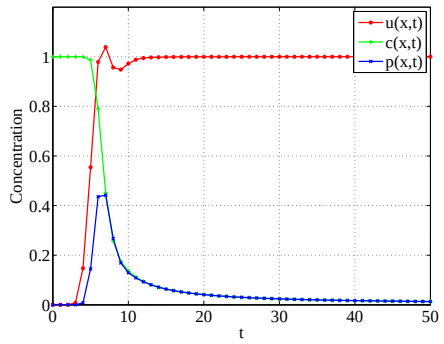
In particular, for Fig. 1, the space grid size was chosen using relation (10) to be

$$\psi(\Delta x) = \Delta x = \sqrt{2\phi(\Delta t)} = \sqrt{2(\exp(0.5) - 1)} =: 1.8538. \tag{20}$$

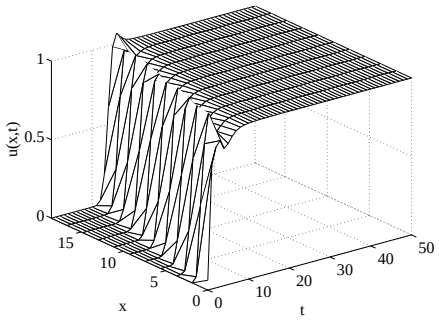
In Figs. 2 and 3 the space step size was chosen arbitrary to be $\Delta x = 1.0$. In Fig. 4, we display simulations for the standard finite difference analogues of schemes (7) , (8) and (12) with $\Delta t = 0.5$. Furthermore, as mentioned earlier, Fig. 5 refers to the NSFD scheme (11) used for classical reaction-diffusion equations. There, with $\psi(\Delta x) = \Delta x = 1$ and keeping the relation (10) in mind, we take

$$u^0(x) = \frac{(x-2)^2}{1+(x-2)^2};\ c^0(x) = \frac{1}{1+x^2} \text{ and } p^0(x) = 0.5u^0(x).$$

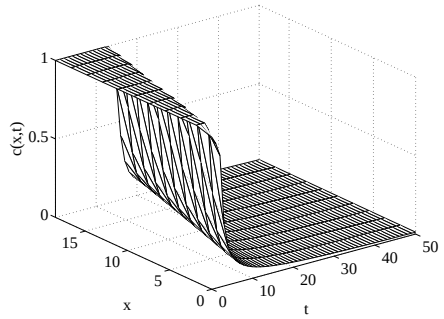
As far as positivity and boundedness of solutions are concerned, it is evident that the NSFD schemes constructed above specifically for the cross-diffusion equations perform better than the standard schemes and the NSFD schemes for classical diffusion equations.



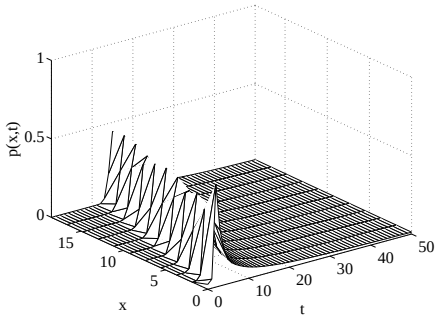

a. All profiles at $x = 5$.




b. Profile $u(x,t)$.

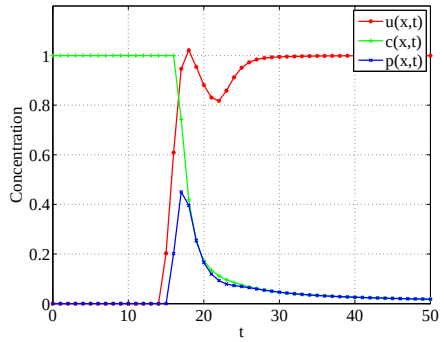



c. Profile $c(x,t)$.

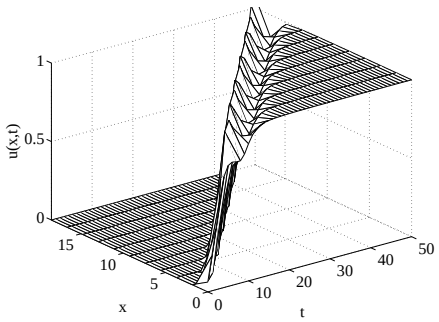



d. Profile $p(x,t)$.

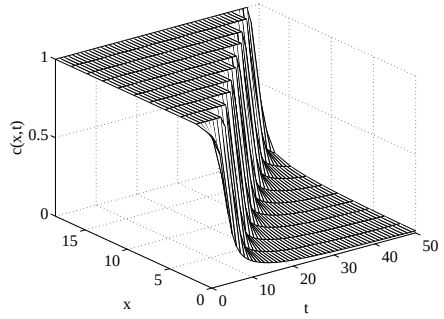
Figure 1: NSFD schemes (7) , (8) with scheme (13) used to solve equation (2).



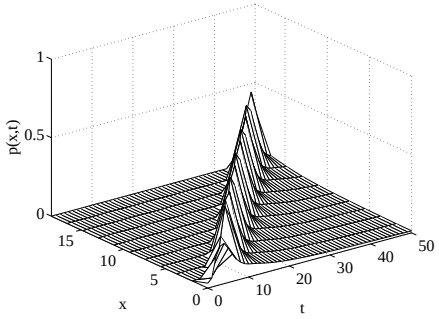

a. All profiles at $x = 5$.




b. Profile $u(x,t)$.

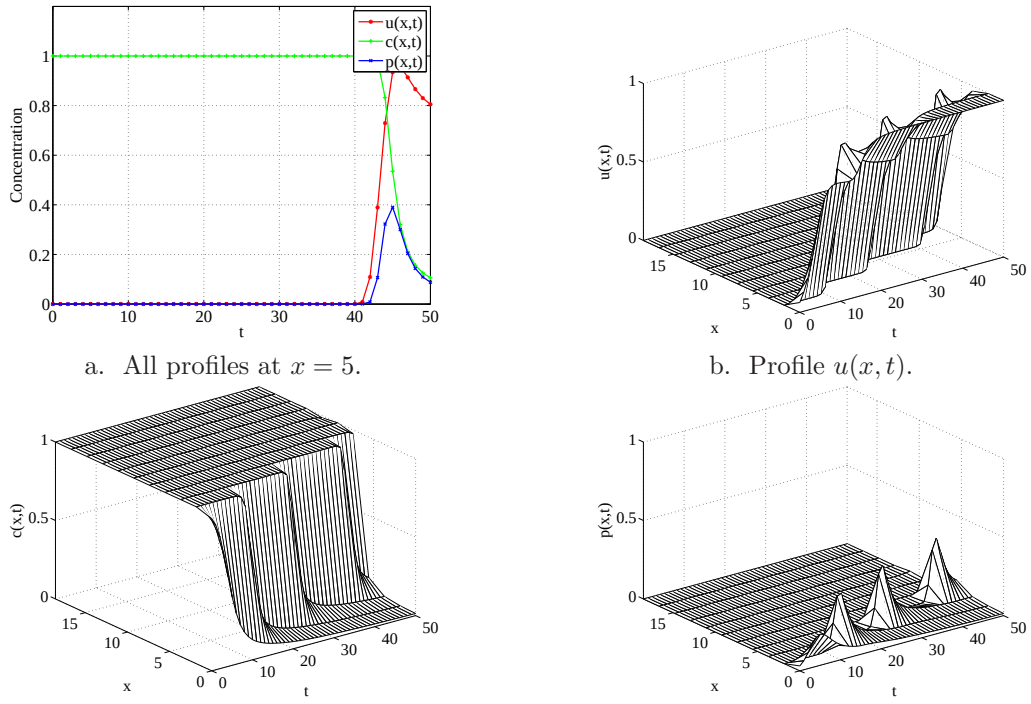



c. Profile $c(x,t)$.




d. Profile $p(x,t)$.

Figure 2: NSFD schemes (7) , (8) with scheme (16) used to solve equation (2).



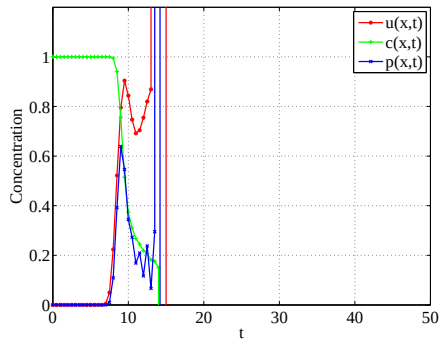

a. All profiles at $x = 5$.

b. Profile $u(x, t)$.

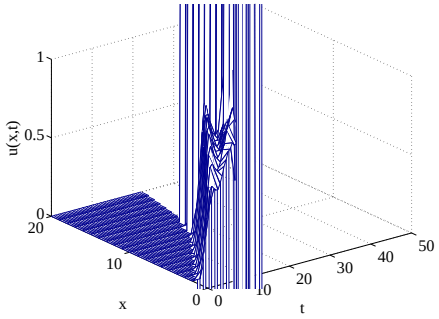
c. Profile $c(x, t)$.

d. Profile $p(x, t)$.

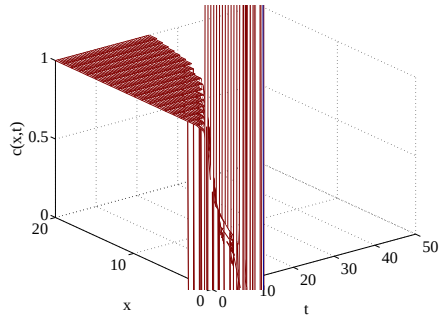
Figure 3: NSFD schemes (7) , (8) with scheme (19) used to solve equation (2).



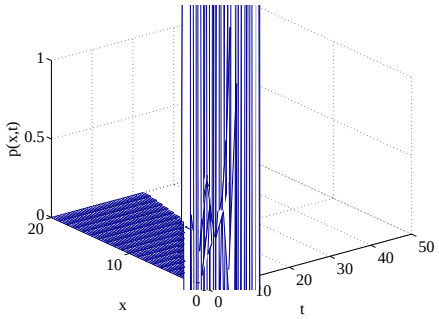

a. All profiles at $x = 5$.




b. Profile $u(x,t)$.




c. Profile $c(x,t)$.




d. Profile $p(x,t)$.

Figure 4: Standard finite difference analogues of the schemes (7) , (8) and (12).

Our numerical simulations have some similarities with those in [10] where very small step sizes are used to study tissue invasion and migration of tumor cells.

| | Scheme (13) | | | Scheme (16) | | | Scheme (19) | | |
|---|---|---|---|---|---|---|---|---|---|
| $\Delta t$ | $u_m^k$ | $c_m^k$ | $p_m^k$ | $u_m^k$ | $c_m^k$ | $p_m^k$ | $u_m^k$ | $c_m^k$ | $p_m^k$ |
| 0.5 | 0.9942 | 0.0822 | 0.0820 | 0.9588 | 0.0998 | 0.0956 | 0.9228 | 0.1106 | 0.1007 |
| 0.25 | 0.9922 | 0.0879 | 0.0881 | 0.9636 | 0.0986 | 0.0957 | 0.9370 | 0.1033 | 0.0972 |
| 0.125 | 0.9857 | 0.0930 | 0.0929 | 0.9695 | 0.0984 | 0.0967 | 0.9512 | 0.1012 | 0.0974 |
| 0.0625 | 0.9708 | 0.0990 | 0.0976 | 0.9725 | 0.0976 | 0.0964 | 0.9587 | 0.0995 | 0.0968 |
| 0.0313 | 0.9471 | 0.1058 | 0.1018 | 0.9741 | 0.0967 | 0.0958 | 0.9626 | 0.0980 | 0.0959 |

Table 1: Convergence of NSFD schemes (7) , (8), (13), (16) and (19).

In Table 1, we demonstrate computationally that the NSFD schemes are convergent: here we take $t^* = 10 = k\Delta t$ with different values of $k \to \infty$ and $\Delta t \to 0$, $x^* = 5 = m\Delta x$, with $m$ changing according to the equation (20) for the scheme (13) and $m = 5$ for schemes (16) and (19). We then tabulate the values of $u_m^k$, $c_m^k$ and $p_m^k$.

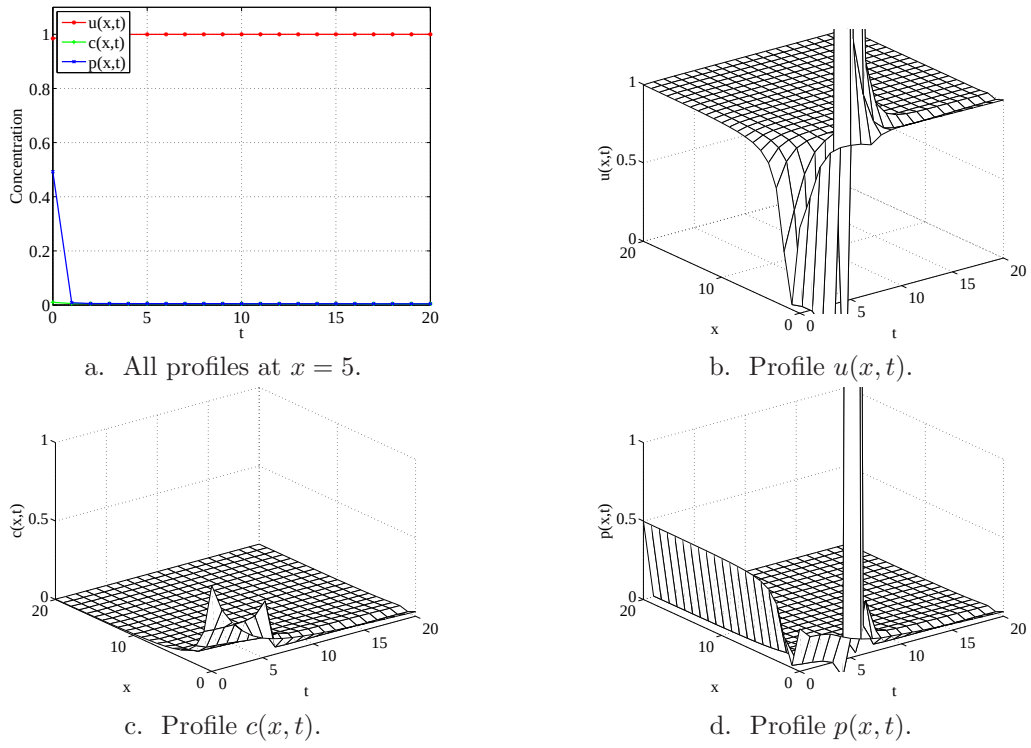
We assume now that the partial derivative $\frac{\partial p}{\partial t}$ is bounded so that

$$p = uc + O(\epsilon).$$

Then, to the leading order of $\epsilon$, the model (2)-(4) is reduced to the system

$$\frac{\partial u}{\partial t} = u(1-u) - \frac{\partial}{\partial x}\left(u\frac{\partial c}{\partial x}\right), \tag{21}$$

$$\frac{\partial c}{\partial t} = -uc^2. \tag{22}$$




a. All profiles at $x = 5$. b. Profile $u(x,t)$.

c. Profile $c(x,t)$. d. Profile $p(x,t)$.

Figure 5: NSFD scheme (11) for classical reaction-diffusion equations

This reduced system is the setting of the study in [14] where traveling wave solutions of the form

$$u(x,t) = U(z) \text{ and } c(x,t) = C(z),\ z = x - at, \tag{23}$$

with speed $a > 0$, and the limit conditions

$$\lim_{z\to-\infty} U(z) = 1,\ \lim_{z\to-\infty} C(z) = 0,\ \lim_{z\to\infty} U(z) = 0 \text{ and } \lim_{z\to\infty} C(z) = \hat{C},$$

for some constant $\hat{C}$, are investigated. We want to demonstrate computationally that the NSFD schemes considered above include the discrete analogue of the traveling wave solutions. To illustrate this fact which was checked for the other scheme, we consider the NSFD scheme (17) or (19) for Eq. (21). Eq. (22) is approximated by

$$\frac{c_m^{k+1} - c_m^k}{\phi(\Delta t)} = -u_m^k c_m^k c_m^{k+1} \text{ or } c_m^{k+1} = \frac{c_m^k}{1 + \phi(\Delta t) u_m^k c_m^k}, \tag{24}$$

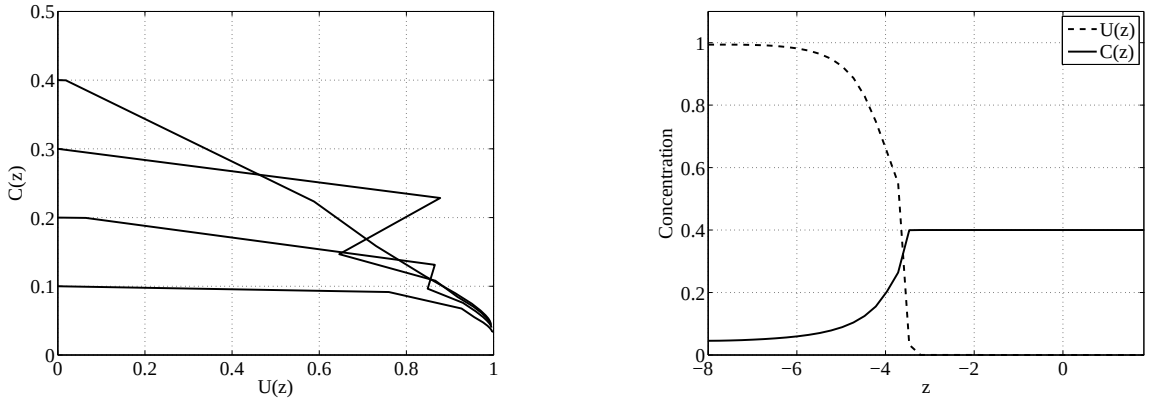
which, like the continuous equation (22), results from plugging into Eq (7) some kind of reduction of Eq (8) to the leading term of $\epsilon$. We assume that the step sizes satisfy the functional relation

$$\Delta x = a\Delta t \tag{25}$$

so that any point $z = x_m - at_k$ coincides with a space grid point: $x_m - at_k = (m-k)\Delta x = x_{m-k}$. Fix the integer $k \geq 0$ and consider the sequences $U(z) := u_m^{k+1}$ and $C(z) := c_m^{k+1}$, in the argument $m \in \mathbb{Z}$, given by Eq (15) and (24), respectively. Alternatively, one can fix $m$ and consider the sequence in $k$. What was mentioned in Remark 3 is once again easily seen here: the defining scheme preserves the equilibrium points of the continuous model, with

$$E_m^* = (U^*, C^*) = (1, 0) \text{ and } E_h^*(U^*, C^*) = (0, \hat{C}) \text{ for any } \hat{C} \geq 0$$

being the only fixed-points. On taking $a = 0.5$ as in [14], but with much larger values of the step sizes namely $\psi(\Delta x) = \Delta x = 1$ and thus $\Delta t = 2$, we obtain simulations that compare with those in this reference. The profile of traveling wave solutions included in the NSFD scheme is shown on Fig. 6(a). The limit set of the positive orbit for the dynamical system that governs the traveling wave solution in (23) contains the unstable malignant steady state $(1, 0)$ and the stable healthy steady state $(0, \hat{C})$. By Poincaré-Bendixon theorem, the limit set contains a trajectory that joins these equilibria. This fact is displayed in Fig. 6. Furthermore, in accordance with [14], the curves start to develop shocks which can also be seen in the full solution on Figs. 2 - 3.




a. Traveling wave solutions. b. Phase-diagram.

Figure 6: NSFD scheme and traveling wave solutions with the phase diagram connections of steady states and shocks.

## 3 Convective predator-prey pursuit and evasion model

Next, we consider the following cross-diffusion equations that model the predator-prey system in which the preys try to evade the predators and the predators try to catch the prey only if they interact [19]:

$$\begin{aligned} \frac{\partial u}{\partial t} - \frac{\partial}{\partial x}[(c_1 + h_1 \frac{\partial v}{\partial x})u] &= (1 - u - v)u \\ \frac{\partial v}{\partial t} - \frac{\partial}{\partial x}[(c_2 - h_2 \frac{\partial u}{\partial x})v] &= (u - 1)v \end{aligned}$$

or equivalently

$$\frac{\partial u}{\partial t} = (1 - u - v)u + (c_1 + h_1 \frac{\partial v}{\partial x})\frac{\partial u}{\partial x} + h_1 u \frac{\partial^2 v}{\partial x^2} \tag{26}$$

$$\frac{\partial v}{\partial t} = (u - 1)v + (c_2 - h_2 \frac{\partial u}{\partial x})\frac{\partial v}{\partial x} - h_2 v \frac{\partial^2 u}{\partial x^2}. \tag{27}$$

Unlike the model in the previous section, the cross-diffusion structure appears in both partial differential equations, with a negative sign in front of at least one of the cross-diffusion terms. Here, $c_1$ and $c_2$ are the speeds of the preys $u$ and predators $v$, in their undisturbed movement. When predators overtake the prey, $c_1 + h_1 \frac{\partial v}{\partial x}$ is the speed of the preys to evade, while $c_2 - h_2 \frac{\partial u}{\partial x}$ is the speed of the predators to move further into the prey. The specific interaction terms $f(u, v) = (1 - u - v)u$ and $g(u, v) = (u - 1)v$ that represent (scaled) population dynamics satisfy the relations $f(u, 0) > f(u, v)$ and $g(u, v) > g(0, v)$ whenever $u$ and $v$ are positive, in accordance with Lotka-Volterra-type model.

For the numerical approximations, we restrict ourselves to the presentation of the approach in (17), though it follows after some computations that the other strategies work and produce unconditionally positivity-preserving NSFD schemes for this model. This yields the following NSFD schemes for Eqs (26) and (27), respectively:

$$\begin{aligned}
\frac{u_m^{k+1}-u_m^k}{\phi(\Delta t)} &= (1-u_m^{k+1})u_m^k - v_m^k u_m^{k+1} + \frac{c_1\psi(\Delta x)u_{m+1}^k + h_1 v_{m+1}^k u_{m+1}^k + h_1 v_{m-1}^k u_m^k}{\psi(\Delta x)^2} \\
&\quad - \frac{c_1\psi(\Delta x)u_m^k + h_1 v_m^k u_{m+1}^k + h_1 v_m^k u_m^k}{\psi(\Delta x)^2} \times \frac{u_m^{k+1}}{u_m^k}, \\
\frac{v_m^{k+1}-v_m^k}{\phi(\Delta t)} &= -v_m^{k+1} + v_m^k u_m^{k+1} + \frac{c_2\psi(\Delta x)v_{m+1}^k + h_2 u_m^k v_{m+1}^k + h_2 u_m^k v_m^k}{\psi(\Delta x)^2} \\
&\quad - \frac{c_2\psi(\Delta x)v_m^k + h_2 u_{m+1}^k v_{m+1}^k + h_2 u_{m-1}^k v_m^k}{\psi(\Delta x)^2} \times \frac{v_m^{k+1}}{v_m^k}
\end{aligned}$$

These schemes are implemented by using their equivalent formulation below in the Gauss-Seidel cycle:

$$u_m^{k+1} = \frac{(1+\phi(\Delta t))u_m^k + R(c_1\psi(\Delta x)u_{m+1}^k + h_1 v_{m+1}^k u_{m+1}^k + h_1 v_{m-1}^k u_m^k)}{1+\phi(\Delta t)(u_m^k+v_m^k) + R(c_1\psi(\Delta x)u_m^k + h_1 v_m^k u_{m+1}^k + h_1 v_m^k u_m^k)/u_m^k}, \tag{28}$$

$$v_m^{k+1} = \frac{v_m^k(1+\phi(\Delta t)u_m^{k+1}) + R(c_2\psi(\Delta x)v_{m+1}^k + h_2 u_m^k v_{m+1}^k + h_2 u_m^k v_m^k)}{1+\phi(\Delta t) + R(c_2\psi(\Delta x)v_m^k + h_2 u_{m+1}^k v_{m+1}^k + h_2 u_{m-1}^k v_m^k)/v_m^k}. \tag{29}$$

The following result is obvious:

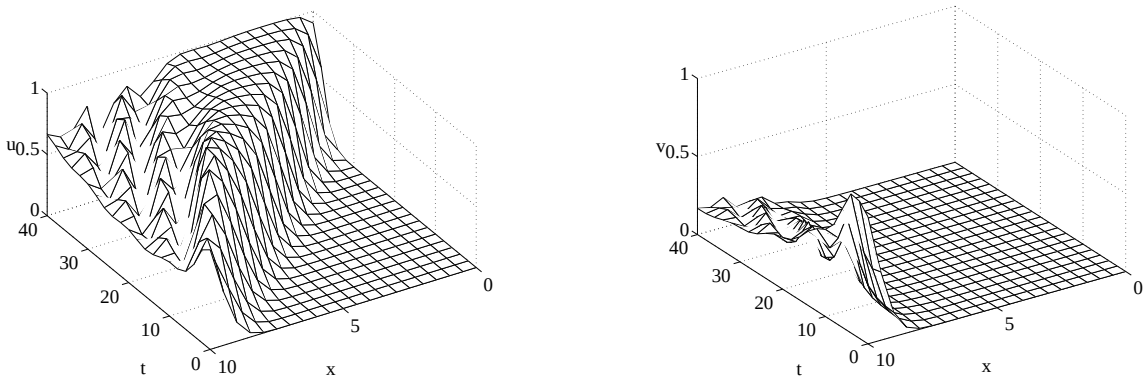
**Theorem 5** *The NSFD scheme preserves the positivity of the continuous solution:*

$$u_m^k \geq 0,\ v_m^k \geq 0 \Longrightarrow u_m^{k+1} \geq 0,\ v_m^{k+1} \geq 0.$$

Theorem 5 is illustrated in Fig. 7 where numerical simulations where obtained with initial condition

$$u^0(x) = v^0(x) = \exp(-x^2).$$

The parameters were chosen as follows: $\Delta t = 2$, $\psi(\Delta x) = \Delta x = 0.5$ and $c_1 = c_2 = h_1 = h_2 = 1$.




a. Profile $u(x,t)$. b. Profile $v(x,t)$.

Figure 7: Profiles for NSFD schemes (28) and (29).

Following [19], the process of pursuit and evasion with variable speeds yields a complex behavior of solutions as seen in Fig. 7. We observed that reducing $\Delta t$ so that the usual stability condition such as $\frac{\Delta t}{(\Delta)^2} \leq \frac{1}{2}$ holds does not remove the complex behavior of solutions (e.g., oscillations, etc). Furthermore, the complex solutions can also be seen from the space independent limit case as shown in Fig. 9 which leads to two equilibria $E_0 = (0,0)$ and $E_1 = (1,0)$, with $E_0$ a saddle point, while the classification of $E_1$ is not clear since one of the eigenvalues of the Jacobian matrix in zero. Please note that [19] anticipates the possibility of shocks. .

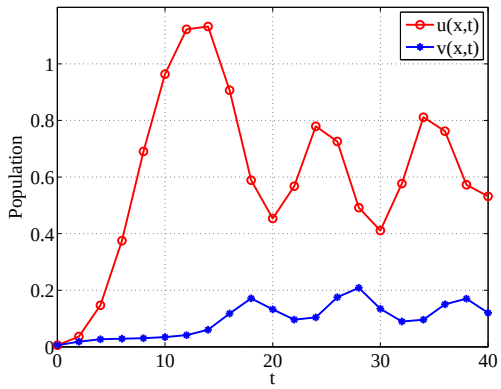



Figure 8: NSFD schemes (28) and (29): the profiles were taken at $x = 8$.

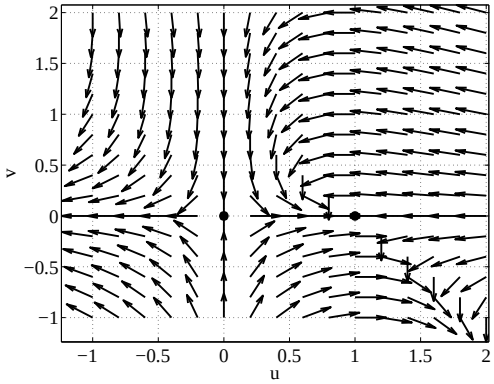



Figure 9: Directional field plots for the space independent limit case.

## 4 Basic reaction-diffusion-chemotaxis model

Our last example of cross-diffusion equations is taken from [18]. We consider the basic reaction-diffusion-chemotaxis equation

$$\frac{\partial n}{\partial t} = \alpha\frac{\partial^2 n}{\partial x^2} - \beta\frac{\partial}{\partial x}(n\frac{\partial a}{\partial x}), \tag{30}$$

$$\frac{\partial a}{\partial t} = hn - \omega a + \gamma\frac{\partial^2 a}{\partial x^2}. \tag{31}$$

Here, chemotaxis refers to the chemically directed movement of a bacterial population $n$ up a gradient in the food (attractant) $a$ that the bacteria consumes. The constant $\alpha$, $\beta$, $\gamma$, $h$ and $\omega$ are positive constants such that $\gamma > \alpha$. Once again, we observe the negative sign in front of the cross-diffusive term.

Eq. (31) is a diffusion equation. Thus following [2], we assume that

$$\psi(\Delta x)^2 = 2\gamma\phi(\Delta t), \text{ i.e. } 2\gamma R = 1, \tag{32}$$

and approximate it by

$$\frac{a_m^{k+1} - a_m^k}{\phi(\Delta t)} = hn_m^k - \omega a_m^{k+1} + \gamma\frac{a_{m+1}^k - 2a_m^k + a_{m-1}^k}{\psi(\Delta x)^2}, \tag{33}$$

or equivalently

$$a_m^{k+1} = \frac{h\phi(\Delta t)n_m^k + (a_{m+1}^k + a_{m-1}^k)/2}{1 + \omega\phi(\Delta t)}. \tag{34}$$

As observed in [16], functional relations of the type (32) between time step size and space step size are essential to reinforce the positivity property of schemes of reaction diffusion equations. However, the presence of the complex denominator functions $\psi$ and $\phi$ makes the condition (32) less restrictive than the classical one $(\Delta x)^2 = 2\gamma\Delta t$ that is needed for stability purposes. For Eq. (31), we use the analogue of (17) for the cross-diffusion term and the analogue of (33) for the diffusion term. This leads to the NSFD scheme

$$\frac{n_m^{k+1}-n_m^k}{\phi(\Delta t)} = \alpha\frac{n_{m+1}^k-2n_m^k+n_{m-1}^k}{\psi(\Delta x)^2} + \beta\frac{(n_m^k+n_{m-1}^k)a_m^k}{\psi(\Delta x)^2} - \beta\frac{n_m^k a_{m+1}^k + n_{m-1}^k a_{m-1}^k}{\psi(\Delta x)^2} \times \frac{n_m^{k+1}}{n_m^k}, \tag{35}$$

which is equivalent to

$$n_m^{k+1} = \frac{(1-2\alpha R)n_m^k + \alpha R(n_{m+1}^k + n_{m-1}^k) + \beta R(n_m^k + n_{m-1}^k)a_m^k}{1+\beta R(n_m^k a_{m+1}^k + n_{m-1}^k a_{m-1}^k)/n_m^k}. \tag{36}$$

In view of the conditions (32) and $\alpha < \gamma$, we have the following result:

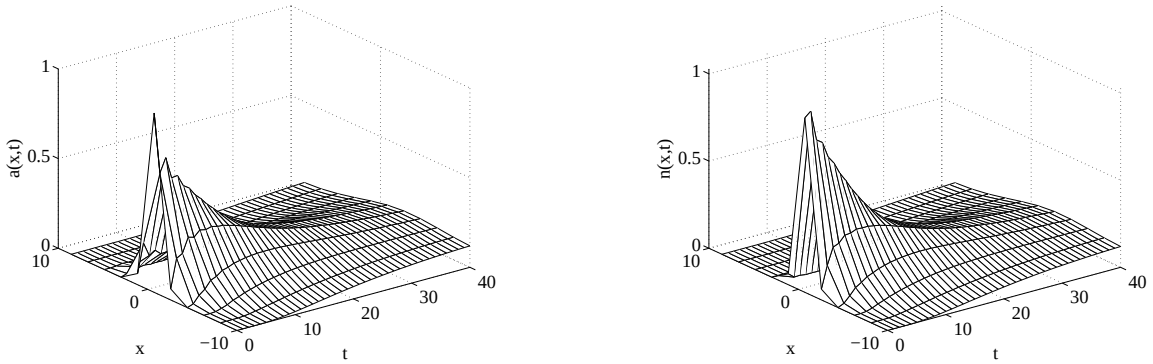
**Theorem 6** *The NSFD scheme (33) and (35) for (30)-(31) preserves the positivity of the continuous solution under the relation (32):*

$$n_m^k \geq 0,\ a_m^k \geq 0 \Longrightarrow n_m^{k+1} \geq 0,\ a_m^{k+1} \geq 0.$$

Theorem 6 is illustrated in Fig. 10 and Fig. 11 where numerical simulations where obtained with initial conditions

$$n^0(x) = a^0(x) = \exp(-x^2).$$

The parameters were chosen as follows: $\Delta t = 2$, and $h = \gamma = \omega = \beta = 1$, $\alpha = 0.5$ and $\psi(\Delta x)$ as in (20).




a. Profile $a(x,t)$. b. Profile $n(x,t)$.

Figure 10: NSFD schemes (34) and (36).

# 5 Conclusion

This paper is motivated by an outstanding problem that was posed by Mickens several years ago and has been recently captured in his edited volume [17]. That is the design of positivity-preserving NSFD schemes for cross-diffusion systems in biosciences.

By a suitable use of Mickens' rules, we have successfully solved the problem in the setting of the following three systems: model of malignant invasion, convective predator-prey pursuit and evasion model and reaction-diffusion-chemotaxis model. In the particular case of the cancer model for which more detail has been given in the paper, we have shown computationally that our NSFD schemes are also dynamically consistent with some of the properties of the traveling wave solutions of the continuous model investigated in [14].

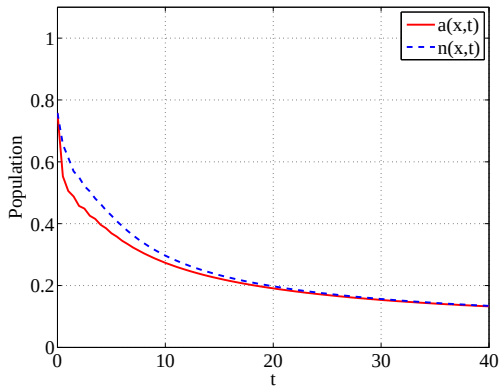



Figure 11: NSFD schemes (34) and (36): the profiles were taken at $x = 6$.

Our immediate interest for future is three-fold. We will study the well-posedness of the models and couple it with the theoretical analysis of the convergence, consistency and stability of the NSFD schemes. Secondly, we plan to incorporate therapy strategies in the model, with the aim of blocking tumor growth and dissemination. As suggested in [20], this amounts to design a mechanism that targets angiogenesis or interrupts blood supply to the solid tumors at their vascular phase. Finally, we will extend this constructive study to the design of dynamically constant NSFD schemes for more complex cancer invasion models such as those that are based on the lymphangiogenesis process [3, 20].

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