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# 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 Marchant et al. (2000).



## 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 [1–4]. 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 [2,3], 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 [5,6], population dynamics via, for instance, Volterra–Lotka cross-diffusion systems [7–9] and chemotaxis [10].

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

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as on their long-time behavior have been established in [7,8]. Equally, the design, for cross-diffusion equations, of reliable numerical methods that produce positive solutions has been an open problem for many years now [11]. The current paper deals precisely with this outstanding problem in the following three settings: a model for cancer growth [12], a convective predator–prey pursuit and evasion model [3] and the basic reaction–diffusion–chemotaxis model [3].

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 [13] 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 [14], 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 [2], 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 [12], 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

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

for $x \in \mathbb{R}$ and $t > 0$. The problem could be considered with appropriate boundary conditions [15].

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 [1,3], that the solutions enjoy the property

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

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 [7,8].