



HAL
open science

Composite waves for a cell population system modelling tumor growth and invasion

Min Tang, Nicolas Vauchelet, Ibrahim Cheddadi, Irene Vignon-Clementel,
Dirk Drasdo, Benoît Perthame

► **To cite this version:**

Min Tang, Nicolas Vauchelet, Ibrahim Cheddadi, Irene Vignon-Clementel, Dirk Drasdo, et al.. Composite waves for a cell population system modelling tumor growth and invasion. Chinese Annals of Mathematics - Series B, 2013, 34B (2), pp.295-318. 10.1007/s11401-007-0001-x . hal-00685063

HAL Id: hal-00685063

<https://hal.science/hal-00685063>

Submitted on 5 Apr 2012

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Composite waves for a cell population system modelling tumor growth and invasion

Min Tang^{*†‡} Nicolas Vauchelet^{§†‡} Ibrahim Cheddadi^{†¶} Irene Vignon-Clementel^{†¶}
Dirk Drasdo[†] Benoît Perthame^{§†}

April 3, 2012

Abstract

The recent biomechanical theory of cancer growth considers solid tumors as liquid-like materials comprising elastic components. In this fluid mechanical view, the expansion ability of a solid tumor into a host tissue is mainly driven by either the cell diffusion constant or the cell division rate, the latter depending either on the local cell density (contact inhibition), on mechanical stress in the tumor, or both.

For the two by two degenerate parabolic/elliptic reaction-diffusion system that results from this modeling, we prove there are always traveling waves above a minimal speed and we analyse their shapes. They appear to be complex with composite shapes and discontinuities. Several small parameters allow for analytical solutions; in particular the incompressible cells limit is very singular and related to the Hele-Shaw equation. These singular traveling waves are recovered numerically.

Key-words: Traveling waves; Reaction-diffusion; Tumor growth; Elastic material;

Mathematical Classification numbers: 35J60; 35K57; 74J30; 92C10;

1 Introduction

Models describing cell multiplication within a tissue are numerous and have been widely studied recently in particular related to cancer invasion. Whereas small-scale phenomena are accurately described by individual-based models (IBM in short, see e.g. [3, 19, 24]), large scale solid tumors can be described by tools from continuum mechanics (see e.g. [6, 2, 15, 17, 18, 16] and [9] for a comparison between IBM and continuum models). The complexity of the subject has led to a number of different approaches and many surveys are now available [1, 4, 32, 5, 21, 25]. They show that the mathematical analysis of these continuum models raises several challenging issues. One of them, which has attracted little attention, is the existence and the structure of traveling waves [12, 15]. This is our main interest here, in particular in the context of fluid mechanical models that have been advocated recently [29, 31]. Traveling wave solutions are of particular interest also from the biological point as the diameter of 2D monolayers, 3D multicellular spheroids and Xenografts, 3D tumors emerging from cells injected into

*Department of mathematics and Institute of Natural Sciences. Shanghai Jiao Tong University

†INRIA Paris Rocquencourt

‡These authors have equally contributed to mathematical analysis

§UPMC Univ Paris 06 and CNRS UMR 7598, Laboratoire Jacques-Louis Lions, F-75005, Paris

¶These authors have equally contributed to modeling

animals is found to increase for many cell lines linearly in time indicating a constant growth speed of the tumor border [30].

In this fluid mechanical view, the expansion ability of tumor cells into a host tissue is mainly driven by cell division rate which depends on the local cell density (contact inhibition) and by mechanical pressure in the tumor [29, 31, 11]. Tumor cells are considered as an elastic material and then respond to pressure by elastic deformation. Denoting by v the velocity field and by ρ the cell population density, we will make use of the following advection-diffusion model :

$$\partial_t \rho + \text{div}(\rho v) - \text{div}(\epsilon \nabla \rho) = \Phi(\rho, \Sigma).$$

In this equation, the third term in the left hand side describes the active motion of cells that results in their diffusion with a nonnegative diffusion coefficient ϵ . The right hand side $\Phi(\rho, \Sigma)$ is the growth term; it expresses that cells divide freely, thus resulting in an exponential growth, as long as the elastic pressure Σ is less than a threshold pressure denoted by C_p where the cell division is stopped by contact inhibition (the term 'homeostatic pressure' has been used for C_p). This critical threshold is determined by the compression that a cell can experience [9]. A simple mathematical representation is

$$\Phi(\rho) = \rho H(C_p - \Sigma(\rho)),$$

where H denotes the Heaviside function : $H(v) = 0$ for $v < 0$ and $H(v) = 1$ for $v > 0$, and $\Sigma(\rho)$ denotes the state equation linking pressure and local cell density. As long as cells are not in contact, the elastic pressure $\Sigma(\rho)$ vanishes whereas it is an increasing function of the population density for larger value of this contact density. Here, after neglecting cell adhesion, we consider the pressure monotonously depending on cell population such that

$$\Sigma(\rho) = 0, \quad \rho \in [0, 1); \quad \Sigma'(\rho) > 0, \quad \rho \geq 1. \quad (1)$$

The flat region $\rho \in [0, 1)$ induces a degeneracy that is one of the interests of the model both for mathematics and biophysical effects; this region represents that cells are too far from and do not touch each other. When elastic deformations are neglected, such as in the incompressible limit of confined cells, this leads to a jump of the pressure from 0 to $+\infty$ at the reference value $\rho = 1$; this highly singular limit leads to Hele-Shaw type of models [28]. Finally the balance of forces acting on the cells lead under certain hypotheses to the following relationship between the velocity field v and the elastic pressure [14]:

$$-C_S \nabla \Sigma(\rho) = -C_z \Delta v + v.$$

This is Darcy's law which describes the tendency of cells to move down pressure gradients, extended to a Brinkman model by a dissipative force density resulting from internal cell friction due to cell volume changes. C_S and C_z are parameters relating respectively the reference elastic and bulk viscosity cell properties with the friction coefficient. The resulting model is then the coupling of this elliptic equation for the velocity field, a conservation equation for the population density of cells and a state equation for the pressure law.

A similar system of equations describing the biomechanical properties of cells has already been suggested as a conclusion in [9] for the radial growth of tumors. That paper proposes to close the system of equations with an elastic fluid model to generalize their derivation for compact tumors that assumed a constant density inside the tumor with a surface tension boundary condition. Many other authors

have also considered such an approach, see e.g. [17, 18]. In [13, 15, 10, 8] cell-cell adhesion is also taken into account, in contrast with equation (1). Their linear stability analysis explains instabilities of the tumor front which are also observed numerically in [15, 13]. However, many of these works focus on nutrient-limited growth whereas we are interested here in stress-regulated growth. Besides, most works deal with a purely elastic fluid model. A viscous fluid model has been motivated in [11, 10, 8] and studied numerically in [8]. Here we include this case in our mathematical study and numerical results. Moreover, we propose here a rigorous analysis of traveling waves which furnishes in some case explicit expressions of the traveling profile and the speed of the wave.

From a mathematical point of view, the description of the invasive ability of cells can be considered as the search of traveling waves. Furthermore the study in several dimensions is also very challenging and we will restrict ourself to the one dimensional case. For reaction-diffusion-advection equations arising from biology, several works have been devoted to the study of traveling waves see for instance [23, 26, 34, 27, 22] and the book [7]. In particular, our model has some formal similarities with the Keller-Segel system with growth treated in [27, 22] with the main difference that the effect of pressure is repulsive here while it is attractive for the Keller-Segel system. More generally, the influence of the physical parameters on the traveling speed is an issue of interest for us and is one of the objectives of this work. Also the complexity of the composite waves arising from different physical effects is an interesting feature of the model at hand. In particular, the nonlinear degeneracy of the diffusion term is an interesting part of the complexity of the phenomena studied here; for instance, as in [33], we construct waves which vanish on the right half-line.

The aim of this paper is to prove the existence of traveling waves above a minimal speed in various situations. For the clarity of the paper, we present our main results in the table below. As mentioned earlier, the incompressible cell limit corresponds to the particular case where the pressure law (1) has a jump from 0 to $+\infty$ when $\rho = 1$.

$C_z = 0$	$\epsilon = 0$	Theorem 3.1
		Incompressible cell limit : Remark 3.4
	$\epsilon > 0$	Theorem 3.5
		Incompressible cell limit : Remark 3.6
$C_z > 0$	$\epsilon = 0$	Incompressible cell limit, $C_S C_p > 2C_z$: Theorem 4.1
		Incompressible cell limit, $C_S C_p < 2C_z$: Remark 4.2
	$\epsilon > 0$	Incompressible cell limit, $C_S C_p > 2C_z$: Theorem 4.4

The outline of this paper is the following. In the next Section, we present some preliminary notations and an a priori estimate resulting on a maximum principle. In Section 3, we investigate the existence of traveling waves in the simplified inviscid case $C_z = 0$, for which the model reduces to a single continuity equation for ρ . Finally, Section 4 is devoted to the study of the general case $C_z \neq 0$ in the incompressible cells limit. In both parts, some numerical simulations illustrate the theoretical results.

2 Preliminaries

In a one dimensional framework, the considerations in the introduction lead to the following set of equations

$$\begin{cases} \partial_t \rho + \partial_x(\rho v) = \Phi(\rho) + \epsilon \partial_{xx} \rho, \\ -C_S \partial_x \Sigma(\rho) = -C_z \partial_{xx} v + v. \end{cases} \quad (2)$$

This system is considered on the whole real line \mathbb{R} and is complemented with Dirichlet boundary conditions at infinity for v and Neumann boundary condition for ρ . Here C_p , C_S , C_z stand for nonnegative rescaled constants. It will be useful for the mathematical analysis to introduce the function W that solves the elliptic problem

$$-C_z \partial_{xx} W + W = \Sigma(\rho), \quad \partial_x W(\pm\infty) = 0.$$

This allows us to set $v = -C_S \partial_x W$ and rewrite the system (2) as

$$\begin{cases} \partial_t \rho - C_S \partial_x(\rho \partial_x W) = \Phi(\rho) + \epsilon \partial_{xx} \rho, \\ -C_z \partial_{xx} W + W = \Sigma(\rho). \end{cases} \quad (3)$$

We recall that the elastic pressure satisfies (1), and the growth function satisfies

$$\Phi(\rho) \geq 0; \quad \Phi(\rho) = 0 \quad \text{for} \quad \Sigma(\rho) \geq C_p > 0. \quad (4)$$

2.1 Maximum principle

The nonlocal aspect of the velocity in term of ρ makes that the correct way to express the maximum principle is not obvious. In particular it does not hold directly on the population density but on the pressure $\Sigma(\rho)$:

Lemma 2.1 *Assume Φ satisfies (4) and that the state equation for Σ satisfies (1). Then setting $\Sigma_M^0 = \max_{x \in \mathbb{R}} \Sigma(x, 0)$, any classical solution of (3) satisfies the maximum principle*

$$\Sigma(\rho) \leq \max(\Sigma_M^0, C_p) \quad \text{and} \quad \rho \leq \Sigma^{-1}(C_p) =: \rho_M > 1 \quad \text{if} \quad \Sigma_M^0 \leq C_p. \quad (5)$$

Notice however that, except in the case when C_z vanishes, this problem is not monotonic, no BV type estimates are available (see [28] for properties when $C_z = 0$).

Proof. Only the values on the intervals such that $\rho > 1$ need to be considered. When $\rho > 1$, multiplying the first equation in (3) by $\Sigma'(\rho)$, we find

$$\frac{\partial}{\partial t} \Sigma(\rho) - C_S \partial_x \Sigma(\rho) \partial_x W - C_S \rho \Sigma'(\rho) \partial_{xx} W = \Sigma'(\rho) \Phi(\rho) + \epsilon \partial_{xx} \Sigma(\rho) - \epsilon \Sigma''(\rho) |\partial_x \rho|^2.$$

Fix a time t , and consider a point x_0 where $\max_x \Sigma(\rho(x, t)) = \Sigma(\rho(x_0, t))$ (the extension to the case that it is not attained is standard [20]). We have $\partial_x \Sigma(\rho(x_0, t)) = 0$, $\partial_{xx} \Sigma(\rho(x_0, t)) \leq 0$ and thus we obtain that

$$\frac{d}{dt} \max_x \Sigma(\rho(x, t)) \leq \Sigma'(\rho(x_0, t)) \Phi(\rho(x_0, t)) + C_S \rho \Sigma'(\rho(x_0, t)) \partial_{xx} W(x_0, t) - \epsilon \Sigma''(\rho(x_0, t)) |\partial_x \rho(x_0, t)|^2.$$

Consider a possible value such that $\Sigma(\rho(x_0, t)) > C_p$. Then we can treat the three terms in the right hands side as follows.

- (i) From assumption (4), we have $\Phi(\rho(x_0, t)) = 0$. And the first term vanishes.
- (ii) Also, by assumption (1), since $\Sigma'(\rho(x_0, t)) > 0$ for $\rho(x_0, t) \geq 1$, we have $\partial_x \rho(x_0, t) = 0$. Therefore the third term vanishes.
- (iii) Moreover, since $-C_z \partial_{xx} W(x_0, t) = \max_x \Sigma(\rho(x, t)) - W(x_0, t) \geq 0$ (by the maximum principle $W \leq \max \Sigma$), using (ii), we conclude that the second term is non-positive.

We conclude that

$$\frac{d}{dt} \max_x \Sigma(\rho(x, t)) \leq 0,$$

and this proves the result. \square

2.2 Traveling waves

The end of this paper deals with existence of a traveling wave for model (3) with the growth term and definition

$$\Phi(\rho) = \rho H(C_p - \Sigma(\rho)), \quad C_p > 0, \quad \rho_M := \Sigma^{-1}(C_p) > 1. \quad (6)$$

There are two constant steady states $\rho = 0$ and $\rho = \rho_M := \Sigma^{-1}(C_p)$ and we look for traveling waves connecting these two stationary states. From Lemma 2.1, we may assume that the initial data satisfies $\max_x \Sigma(\rho(x, t = 0)) = C_p$ and $\max_x \rho(x, t = 0) = \rho_M$; then, it is natural to define :

Definition 2.2 *A non-increasing traveling wave solution is a solution of the form $\rho(t, x) = \rho(x - \sigma t)$ for $\sigma \in \mathbb{R}$ a constant called the traveling speed, such that $\rho' \leq 0$, $\rho(-\infty) = \rho_M$ and $\rho(+\infty) = 0$.*

With this definition, we are led to look for (ρ, W) satisfying

$$-\sigma \partial_x \rho - C_S \partial_x (\rho \partial_x W) = \rho H(C_p - \Sigma(\rho)) + \epsilon \partial_{xx} \rho, \quad (7)$$

$$-C_z \partial_{xx} W + W = \Sigma(\rho), \quad (8)$$

$$\rho(-\infty) = \rho_M, \quad \rho(+\infty) = 0; \quad W(-\infty) = C_p, \quad W(+\infty) = 0. \quad (9)$$

When $C_z = 0$, system (7)–(8) reduces to one single equation

$$-\sigma \partial_x \rho - C_S \partial_x (\rho \partial_x \Sigma(\rho)) = \rho H(C_p - \Sigma(\rho)) + \epsilon \partial_{xx} \rho. \quad (10)$$

In the sequel and in order to make the mathematical analysis more tractable, as depicted in Figure 1, we assume that Σ has the specific form given by

$$\Sigma(\rho) = \begin{cases} 0 & \text{for } \rho \leq 1, \\ C_\nu \ln \rho & \text{for } \rho \geq 1. \end{cases} \quad (11)$$

This form represents logarithmic strain assuming cells of cuboidal shape (see Appendix). The choice of logarithmic strain conserves the volume of incompressible cells for both small and large deformations. Hence it is particularly useful as cells, because they are mainly composed of water, are incompressible on small time scales such that deformations leave cell volume invariant.

We will study in particular the case $C_\nu \rightarrow +\infty$, we call it the incompressible cell limit, which is both mathematically interesting (see also the derivation of Hele-Shaw equation in [28]) and physically relevant; this limit case boils down to consider tumor cells tissue as an incompressible elastic material in a confined environment.

The structure of the problem (2) depends deeply on the parameters ϵ and C_z . It is hyperbolic for $\epsilon = C_z = 0$, and parabolic when $\epsilon \neq 0$, $C_z = 0$ and coupled parabolic/elliptic in the general case. Therefore we have to treat each case separately.

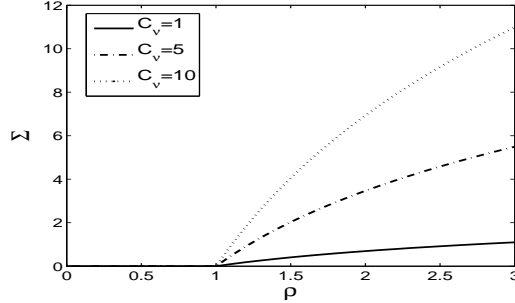


Figure 1: The equation of state as defined by (11) for three different values of C_ν .

3 Traveling wave without viscosity

When the bulk viscosity is neglected, that is $C_z = 0$, the analysis is much simpler and is closely related to the Fisher/KPP equation [7] with the variant of a complex composite and discontinuous wave. The unknown W can be eliminated and, taking advantage of the state equation for the pressure (11), we can rewrite equation (10) as a self-contained equation on ρ

$$\begin{cases} -\sigma \partial_x \rho - C_S C_\nu \partial_{xx} Q(\rho) = \rho H(C_p - C_\nu (\ln \rho)_+) + \epsilon \partial_{xx} \rho, \\ \rho(-\infty) = \rho_M, \quad \rho(+\infty) = 0. \end{cases} \quad (12)$$

Here f_+ denotes the positive part of f and

$$Q(\rho) = \begin{cases} 0 & \text{for } \rho \leq 1, \\ \rho - 1 & \text{for } \rho \geq 1. \end{cases} \quad (13)$$

3.1 Traveling waves for $\epsilon = 0$

When cell motility is neglected, we can find explicit expression for the traveling waves. More precisely, we establish the following result :

Theorem 3.1 *There exists $\sigma^* > 0$ such that for all $\sigma \geq \sigma^*$, (12)–(13) admits a nonnegative, non-increasing and discontinuous solution ρ . More precisely, when $\sigma = \sigma^*$ and up to translation, ρ is given by*

$$\rho(x) = \begin{cases} \rho_M := \exp\left(\frac{C_p}{C_\nu}\right) & x \leq 0, \\ g(x) & x \in (0, x_0), \quad x_0 > 0, \\ 0 & x > x_0, \end{cases}$$

where g is a smooth non-increasing function satisfying $g(0) = \rho_M$, $g'(0) = 0$ and $g(x_0) = 1$; its precise expression is given in the proof.

In other words, when $C_z = 0$ and $\epsilon = 0$, system (3) admits a nonnegative and non-increasing traveling wave (ρ, W) for $\sigma \geq \sigma^*$.

Notice that, by opposition to the Fisher/KPP equation we do not have an analytical expression for the minimal speed. Related is that ρ vanishes for x large, a phenomena already known for degenerate diffusion.

Proof. Since we are looking for a non-increasing function ρ , we decompose the line as

$$\mathbb{R} = I_1 \cup I_2 \cup I_3, \quad I_1 = \{\rho(x) = \rho_M\}, \quad I_2 = \{1 < \rho(x) < \rho_M\}, \quad I_3 = \{\rho(x) \leq 1\}.$$

Notice that, equivalently $\Sigma(x) = C_p$ in I_1 . To fix the notations, we set

$$I_1 = (-\infty, 0], \quad I_2 = (0, x_0), \quad I_3 = [x_0, +\infty).$$

First step. In $I_1 \cup I_2$: ρ satisfies

$$-\sigma \partial_x \rho - C_S C_\nu \partial_{xx} \rho = \rho H(C_p - C_\nu (\ln \rho)_+). \quad (14)$$

Therefore by elliptic regularity, we deduce that the second derivative of ρ is bounded and therefore $\rho \in C^1(-\infty, x_0)$. On I_1 , the function ρ is a constant and by continuity of ρ and $\partial_x \rho$ at $x = 0$, we have the boundary conditions of I_2 such that

$$\rho(0) = \rho_M, \quad \partial_x \rho(0) = 0. \quad (15)$$

On I_2 , $H(C_p - C_\nu (\ln \rho)_+) = 1$. Solving (14) with the boundary conditions in (15), we find that if $\sigma > 2\sqrt{C_S C_\nu}$, then

$$\rho(x) = \rho_M e^{-\sigma x / (2C_S C_\nu)} \left(A \exp\left(\frac{\sqrt{\sigma^2 - 4C_S C_\nu}}{2C_S C_\nu} x\right) + B \exp\left(-\frac{\sqrt{\sigma^2 - 4C_S C_\nu}}{2C_S C_\nu} x\right) \right),$$

with

$$A = \frac{\sigma + \sqrt{\sigma^2 - 4C_S C_\nu}}{2\sqrt{\sigma^2 - 4C_S C_\nu}}, \quad B = \frac{-\sigma + \sqrt{\sigma^2 - 4C_S C_\nu}}{2\sqrt{\sigma^2 - 4C_S C_\nu}}.$$

In this case, ρ is decreasing for $x > 0$ and vanishes as $x \rightarrow +\infty$, thus there exists a positive x_0 such that $\rho(x_0) = 1$.

When $\sigma < 2\sqrt{C_S C_\nu}$, the solution writes

$$\rho(x) = \rho_M e^{-\sigma x / (2C_S C_\nu)} \left(A \cos\left(\frac{\sqrt{4C_S C_\nu - \sigma^2}}{2C_S C_\nu} x\right) + B \sin\left(\frac{\sqrt{4C_S C_\nu - \sigma^2}}{2C_S C_\nu} x\right) \right), \quad (16)$$

with

$$A = 1, \quad B = \frac{\sigma}{\sqrt{4C_S C_\nu - \sigma^2}}.$$

By a straightforward computation, we deduce,

$$\partial_x \rho(x) = -\frac{2\rho_M}{\sqrt{4C_S C_\nu - \sigma^2}} e^{-\sigma x / (2C_S C_\nu)} \sin\left(\frac{\sqrt{4C_S C_\nu - \sigma^2}}{2C_S C_\nu} x\right).$$

Thus ρ is decreasing on $(0, \frac{2C_S C_\nu}{\sqrt{4C_S C_\nu - \sigma^2}} \pi)$ and takes negative values at the largest endpoint. There exists $x_0 > 0$ such that $\rho(x_0) = 1$.

Finally, when $\sigma = 2\sqrt{C_S C_\nu}$, we reach the same conclusion because

$$\rho(x) = \rho_M \left(\frac{x}{\sqrt{C_S C_\nu}} + 1 \right) e^{-x/\sqrt{C_S C_\nu}}.$$

Second step. On I_3 : on $(x_0, +\infty)$, we have $\Sigma = 0$ and $Q(\rho) = 0$ from (13), then equation (12) writes

$$-\sigma \partial_x \rho = \rho. \quad (17)$$

We can write the jump condition at x_0 by integrating (12) from x_0^- to x_0^+ , which is

$$-\sigma[\rho]_{x_0} - C_S C_\nu [\partial_x Q(\rho)]_{x_0} = 0, \quad \sigma(\rho(x_0^+) - 1) = C_S C_\nu \partial_x \rho(x_0^-).$$

Here $\partial_x \rho(x_0^-) < 0$ can be found thanks to the expression of ρ on I_2 as computed above. Thus, we get $\rho(x_0^+)$, which is the boundary condition of (17). Then the Cauchy problem (17) gives

$$\rho(x) = \left(1 + \frac{C_S C_\nu}{\sigma} \partial_x \rho(x_0^-) \right) e^{-x/\sigma}, \quad x \in I_3.$$

In summary, when $\epsilon = 0$, a nonnegative solution to (12) exists under the necessary and sufficient condition

$$\sigma \geq -C_S C_\nu \partial_x \rho(x_0^-). \quad (18)$$

The right hand side also depends on σ , therefore it does not read obviously $\sigma \geq \sigma^*$. To reach this conclusion, and conclude the proof, we shall use Lemma 3.2 below. \square

Lemma 3.2 *Using the notation in the proof of Theorem 3.1, the function $\sigma \mapsto -C_S C_\nu \partial_x \rho(x_0^-)$ is nonincreasing. Therefore there exists a minimal traveling wave velocity σ^* , and (18) is satisfied if and only if $\sigma \geq \sigma^*$.*

Proof. We consider equation (14) on $I_2 = (0, x_0)$. We notice that on this interval, $\rho(x)$ is decreasing and therefore is one to one from $(0, x_0)$ to $(\rho_M, 1)$; we denote by $X(\rho)$ its inverse. Let us define $V = -C_S C_\nu \partial_x \rho$. On I_2 , V is nonnegative and (14) can be written as

$$\partial_x V = \sigma \partial_x \rho + \rho = -\frac{V}{C_S C_\nu} \sigma + \rho. \quad (19)$$

Setting $\tilde{V}(\rho) = V(X(\rho))$, by definition of V , we have

$$\partial_\rho \tilde{V} = \partial_x V \partial_\rho X = \partial_x V / \partial_x \rho = -\partial_x V \frac{C_S C_\nu}{V}.$$

By using (19), we finally get the differential equation

$$\begin{cases} \partial_\rho \tilde{V} = \sigma - \frac{C_S C_\nu \rho}{\tilde{V}}, & \text{for } \rho \in (1, \rho_M), \\ \lim_{\rho \rightarrow \rho_M} \tilde{V}(\rho_M) = -C_S C_\nu \partial_x \rho(0) = 0. \end{cases} \quad (20)$$

This differential equation has a singularity at ρ_M . We introduce then $z = \rho_M - \rho$ and $Y(z) = \frac{1}{2} \tilde{V}^2(\rho_M - z)$ for $z \in (0, \rho_M - 1)$. Equation (20) becomes

$$\begin{cases} Y'(z) = -\sigma \sqrt{2Y(z)} + C_S C_\nu (\rho_M - z), & \text{for } z \in (0, \rho_M - 1), \\ Y(0) = 0. \end{cases}$$

This ordinary differential equation belongs to the class $Y' = F(z, Y)$ with F one sided Lipschitz in his second variable and $\partial_Y F(z, Y) \leq 0$. Therefore we can define a unique solution to the above Cauchy problem. Hence there exists a unique nonnegative solution \tilde{V} of (20).

Define $U(\rho) := \frac{\partial \tilde{V}}{\partial \sigma}$, our goal is to determine the sign of $U(1)$. We have

$$\frac{\partial^2 \tilde{V}}{\partial \rho \partial \sigma} = \frac{\partial}{\partial \sigma} \left(\sigma - \frac{C_S C_\nu}{\tilde{V}} \rho \right) = 1 + \frac{C_S C_\nu}{\tilde{V}^2} \rho \frac{\partial \tilde{V}}{\partial \sigma}.$$

Then $U(\rho)$ solves on $(1, \rho_M)$

$$\frac{\partial U}{\partial \rho} = 1 + \frac{C_S C_\nu}{\tilde{V}^2} \rho U. \quad (21)$$

Moreover, we have

$$U(\rho_M) = \frac{\partial \tilde{V}(\rho_M)}{\partial \sigma} = 0. \quad (22)$$

Assume $U(1) > 0$, and let us define $\rho_1 = \sup\{\rho_2 | \rho \in (1, \rho_2) \text{ such that } U(\rho) \geq 0\}$. Then from (21), $\frac{\partial U}{\partial \rho}(\rho) \geq 1$ on $(1, \rho_1)$, thus $U(\rho_1) > U(1) > 0$. By continuity, we should necessarily have $\rho_1 = \rho_M$. However, we have then $\frac{\partial U}{\partial \rho}(\rho) \geq 1$ for all $\rho \in (1, \rho_M)$ which is a contradiction to $U(\rho_M) = 0$. Therefore, $U(1) \leq 0$ and \tilde{V} is nonincreasing with respect to σ . \square

Structural stability. Theorem 3.1 shows that there are an infinity of traveling wave solutions. However, as in the Fisher/KPP equation, most of them are unstable. For instance, we can consider some kind of 'ignition temperature' approximation to the system (12) such that

$$-\sigma \partial_x \rho_\theta - C_S C_\nu \partial_{xx} Q(\rho_\theta) = \xi_\theta(\rho_\theta) H(C_p - C_\nu(\ln \rho_\theta)_+), \quad (23)$$

where $\theta \in (0, 1)$ is a small positive parameter and

$$\xi_\theta(\rho) = \begin{cases} \rho & \text{for } \rho \in (\theta, \rho_M), \\ 0 & \text{for } \rho \in [0, \theta]. \end{cases} \quad (24)$$

Then we have the

Lemma 3.3 *Equation (23)-(24) admits an unique couple of solution $(\sigma_\theta, \rho_\theta)$ and $\sigma_\theta \rightarrow \sigma^*$ as $\theta \rightarrow 0$.*

Proof. As in Theorem 3.1, we solve (23) by using the decomposition $\mathbb{R} = I_1 \cup I_2 \cup I_3$. On $I_1 \cup I_2$, $\rho \geq 1 > \theta$, therefore ρ is given by the same formula as computed in the proof of Theorem 3.1. On I_3 , equation (23) becomes

$$-\sigma_\theta \partial_x \rho_\theta = \xi_\theta(\rho_\theta). \quad (25)$$

By contradiction, if $\rho_\theta(x_0^+) \geq \theta$, then equation (25) implies $\rho_\theta(x) = \rho_\theta(x_0^+) e^{-(x-x_0)/\sigma}$. Thus there exists x_θ such that $\rho_\theta(x) \leq \theta$ for $x \geq x_\theta$. Then the right hand side of (25) vanishes for $x \geq x_\theta$ and ρ_θ is constant for $x \geq x_\theta$. This constant has to vanish from the condition at infinity which contradicts the continuity of ρ_θ . Thus, $\rho_\theta(x_0^+) < \theta$ and equation (25) implies that $\partial_x \rho_\theta = 0$. We conclude that $\rho_\theta = 0$ on I_3 . The jump condition at the interface $x = x_0$ gives

$$\sigma_\theta(\rho_\theta(x_0^+) - 1) = C_S C_\nu \partial_x \rho_\theta(x_0^-),$$

which, together with $\rho(x_0^+) = 0$, indicates that

$$\sigma_\theta = -C_S C_\nu \partial_x \rho_\theta(x_0^-).$$

According to Lemma 3.2, there exists an unique σ_θ^* satisfying the equality above, so that an unique ρ_θ .

Letting $\theta \rightarrow 0$ in this formula, we recover the equality case in (18) that defines the minimal speed in Theorem 3.1. By continuity of the unique solution, we find $\sigma_\theta \rightarrow \sigma^*$. \square

Remark 3.4 (incompressible cells limit) *In the incompressible cells limit $C_\nu \rightarrow +\infty$, we can obtain an explicit expression of the traveling wave from theorem 3.1. Since $\rho_M = \exp(C_p/C_\nu) \rightarrow 1$, we have $\rho(x) \rightarrow 1$ on $I_1 \cup I_2$ but Σ carries more structural information. In the first step of the proof we are led, for C_ν large, to use (16) and we find*

$$\Sigma(x) = C_\nu \ln(\rho) \rightarrow C_p - \frac{x^2}{2C_S}.$$

We recall that the point x_0 is such that $\rho(x_0) = 1$ or $\Sigma(x_0) = 0$. Therefore $x_0 = \sqrt{2C_S C_p}$ and

$$C_\nu \partial_x \rho(x_0^-) = \partial_x \Sigma(x_0^-) \rightarrow -\sqrt{\frac{2C_p}{C_S}}, \quad \text{as } C_\nu \rightarrow +\infty.$$

Thus $\sigma^* \rightarrow \sqrt{2C_p C_S}$ and we conclude that, on $I_3 = [x_0, +\infty)$, $\rho(x) \rightarrow \left(1 - \frac{\sqrt{2C_p C_S}}{\sigma}\right) e^{-x/\sigma}$.

3.2 Traveling wave when $\epsilon \neq 0$

We can extend Theorem 3.1 to the case $\epsilon \neq 0$.

Theorem 3.5 *There exists $\sigma^* > 2\sqrt{\epsilon}$ such that for all $\sigma \geq \sigma^*$, (12)–(13) admits a nonnegative, non-increasing and continuous solution ρ .*

Thus when $C_z = 0$, system (3) admits a nonnegative and non-increasing traveling wave (ρ, W) for $\sigma \geq \sigma^$.*

Proof. We follow the proof of Theorem 3.1 and decompose $\mathbb{R} = I_1 \cup I_2 \cup I_3$. Due to the diffusion term in (12), $\rho \in C^0(\mathbb{R})$ and we will use the continuity of ρ at the interfaces.

On $I_1 = (-\infty, 0]$: we have $\rho = \rho_M$ and $\Sigma = C_p$.

On $I_2 = (0, x_0)$: equation (12) writes

$$(C_S C_\nu + \epsilon) \partial_{xx} \rho + \sigma \partial_x \rho + \rho = 0, \quad \rho(0) = \rho_M, \quad \partial_x \rho(0) = 0.$$

We get therefore the same expressions for ρ on I_2 as in the proof of Theorem 3.1 except that we replace $C_S C_\nu$ by $C_S C_\nu + \epsilon$. Thus, as before, there exists a positive x_0 such that $\rho(x_0) = 1$ and ρ is decreasing on $(0, x_0)$.

On $I_3 = [x_0, +\infty)$: we solve

$$\epsilon \partial_{xx} \rho + \sigma \partial_x \rho + \rho = 0. \tag{26}$$

At the interface $x = x_0$, integrating from x_0^- to x_0^+ in (12) and using the continuity of ρ , we get

$$C_S C_\nu [\partial_x Q(\rho)]_{x_0} + \epsilon [\partial_x \rho]_{x_0} = 0,$$

that is

$$\partial_x \rho(x_0^+) = \left(1 + \frac{C_S C_\nu}{\epsilon}\right) \partial_x \rho(x_0^-). \tag{27}$$

Solving equation (26) with the boundary conditions $\rho(x_0^+) = 1$ and (27), we get that if $\sigma < 2\sqrt{\epsilon}$, then ρ is the sum of trigonometric function and therefore will take negative values. Thus $\sigma \geq 2\sqrt{\epsilon}$. In the case $\sigma > 2\sqrt{\epsilon}$,

$$\rho(x) = A \exp\left(\frac{-\sigma + \sqrt{\sigma^2 - 4\epsilon}}{2\epsilon}(x - x_0)\right) + B \exp\left(\frac{-\sigma - \sqrt{\sigma^2 - 4\epsilon}}{2\epsilon}(x - x_0)\right),$$

where

$$A = \frac{1}{2} + \frac{1}{\sqrt{\sigma^2 - 4\epsilon}} \left(\frac{\sigma}{2} + (\epsilon + C_S C_\nu) \partial_x \rho(x_0^-) \right), \quad B = \frac{1}{2} - \frac{1}{\sqrt{\sigma^2 - 4\epsilon}} \left(\frac{\sigma}{2} + (\epsilon + C_S C_\nu) \partial_x \rho(x_0^-) \right).$$

After detailed calculation of $\partial_x \rho$ and using $\partial_x \rho(x_0^-) < 0$, we have that ρ is a nonnegative and non-increasing function if and only if $A \geq 0$, that is

$$\sqrt{\sigma^2 - 4\epsilon} + \sigma + 2(\epsilon + C_S C_\nu) \partial_x \rho(x_0^-) \geq 0, \quad \sigma > 2\sqrt{\epsilon}. \quad (28)$$

In the case $\sigma = 2\sqrt{\epsilon}$, we have

$$\rho(x) = \left(\left(\frac{1}{\sqrt{\epsilon}} + \left(1 + \frac{C_S C_\nu}{\epsilon}\right) \partial_x \rho(x_0^-) \right) (x - x_0) + 1 \right) e^{-(x-x_0)/\sqrt{\epsilon}}.$$

Thus ρ is a nonnegative and non-increasing function if and only if

$$\frac{1}{\sqrt{\epsilon}} + \left(1 + \frac{C_S C_\nu}{\epsilon}\right) \partial_x \rho(x_0^-) \geq 0,$$

which is the same condition as (28) by setting $\sigma = 2\sqrt{\epsilon}$. Thus (28) is valid for $\sigma \geq 2\sqrt{\epsilon}$. Denoting $U_\epsilon(x) = -(\epsilon + C_S C_\nu) \partial_x \rho(x)$, condition (28) can be rewritten into

$$\sigma \geq \mathfrak{F}[\sigma] := \max \left(2\sqrt{\epsilon}, \min \left(2U_\epsilon(x_0^-), U_\epsilon(x_0^-) + \frac{\epsilon}{U_\epsilon(x_0^-)} \right) \right). \quad (29)$$

By a straightforward adaptation of Lemma 3.2, we conclude that $\sigma \mapsto U_\epsilon(x_0^-)$ is nonincreasing with respect to σ . When $U_\epsilon(x_0^-) > \sqrt{\epsilon}$, we have $\mathfrak{F}[\sigma] = U_\epsilon(x_0^-) + \frac{\epsilon}{U_\epsilon(x_0^-)}$. Then $\mathfrak{F}[\sigma]$ is an increasing function with respect to $U_\epsilon(x_0^-)$ for $U_\epsilon(x_0^-) > \sqrt{\epsilon}$. Together with $\sigma \rightarrow U_\epsilon(x_0^-)$ is nonincreasing, $\mathfrak{F}[\sigma]$ is nonincreasing with respect to σ . For the case $U_\epsilon(x_0^-)^2 < \epsilon$, we have $\mathfrak{F}[\sigma] = 2\sqrt{\epsilon}$. Therefore for all $\sigma \in (0, +\infty)$, $\mathfrak{F}[\sigma]$ is a non-increasing function of σ . Hence there exists a unique σ^* such that (29) is satisfied for every $\sigma \geq \sigma^*$. \square

Structural stability. We can again select a unique traveling wave when approximating the growth term by $\xi_\theta(\rho)H(C_p - C_\nu(\ln \rho)_+)$. This can be obtained by considering $\epsilon \partial_{xx} \rho_\theta + \sigma \partial_x \rho_\theta + \xi_\theta(\rho_\theta) = 0$ instead of (26) and matching the values of $\partial_x \rho$ on both sides at the point where $\rho = \theta$. Then, the equality in (28) holds and one unique velocity is selected. As for (23), we let $\theta \rightarrow 0$ and the minimum traveling velocity σ^* is selected. Then

Remark 3.6 (incompressible cells limit) In the limit $C_\nu \rightarrow +\infty$, we have $\rho(x) \rightarrow 1$ on $I_2 = (0, x_0)$ and

$$\Sigma(x) = C_\nu \ln(\rho) \rightarrow C_p - \frac{x^2}{2C_S}.$$

Therefore $x_0 = \sqrt{2C_S C_p}$ and

$$C_\nu \partial_x \rho(x_0^-) = \partial_x \Sigma(x_0^-) \rightarrow -\sqrt{\frac{2C_p}{C_S}}, \quad \text{when } C_\nu \rightarrow +\infty.$$

Thus equation (28) becomes, for $\sigma \geq 2\sqrt{\epsilon}$,

$$\sqrt{\sigma^2 - 4\epsilon} + \sigma \geq 2\sqrt{2C_p C_S},$$

and we conclude, in this incompressible cells limit, that σ^* is defined by

$$\sigma^* := \max \left(2\sqrt{\epsilon}, \min \left(2\sqrt{2C_p C_S}, \sqrt{2C_p C_S} + \frac{\epsilon}{\sqrt{2C_p C_S}} \right) \right). \quad (30)$$

The kink induced by this formula is a very typical qualitative feature that is recovered in numerical simulations (see Table 1 below).

3.3 Numerical results

In order to perform numerical simulations, we consider a large computational domain $\Omega = [-L, L]$ and we discretize it with a uniform mesh

$$\Delta x = \frac{L}{2M}, \quad x_i = i\Delta x, \quad i = -M, \dots, 0, \dots, M.$$

We simulate the time evolutionary Equation (3) with $C_z = 0$ and Neumann boundary conditions. Our algorithm is based on a splitting method. Firstly, we discretize $\partial_t \rho - C_S \partial_{xx} Q(\rho) = 0$ using explicit Euler method in time and second order centered finite differences in space. After updating ρ^n for one time step, we denote the result by $\rho^{n+1/2}$. Secondly, we solve $\partial_t \rho = \rho H(C_p - \Sigma(\rho))$ by explicit Euler scheme again, using $\rho^{n+1/2}$ as the initial condition; we get ρ^{n+1} .

The numerical initial density ρ is a small Gaussian in the center of the computational domain and we take

$$L = 3, \quad C_\nu = 17.114, \quad C_S = 0.01, \quad C_p = 1. \quad (31)$$

The numerical traveling wave solution when $C_z = 0, \epsilon = 0$ is depicted in Figure 2. We can see that two fronts propagate in opposite direction with constant speed. The right propagating front of ρ has a jump from 1 to 0, whereas Σ is continuous, but its derivative $\partial_x \Sigma$ has a jump at the front. Figure 3 presents the numerical results of $C_z = 0, \epsilon = 0.02$, where ρ becomes continuous and the front shape of Σ keeps the same as for $\epsilon = 0$. Comparing Figure 2 and Figure 3, when there is diffusion, the traveling velocity becomes bigger and the density has a tail.

The numerical traveling velocities for different parameters are given in Table 1, where we can compare with the analytical formula (30) in the incompressible cells limit.

4 Traveling wave with viscosity

When $C_z \neq 0$, we cannot eliminate an unknown and we have to deal with the whole system

$$\begin{cases} -\sigma \partial_x \rho - C_S \partial_x \rho \partial_x W - C_S \rho \partial_{xx} W = \rho H(C_p - \Sigma) + \epsilon \partial_{xx} \rho, \\ -C_z \partial_{xx} W + W = \Sigma(\rho), \\ \rho(-\infty) = \rho_M, \quad \rho(+\infty) = 0; \quad W(-\infty) = C_p, \quad W(+\infty) = 0, \end{cases} \quad (32)$$

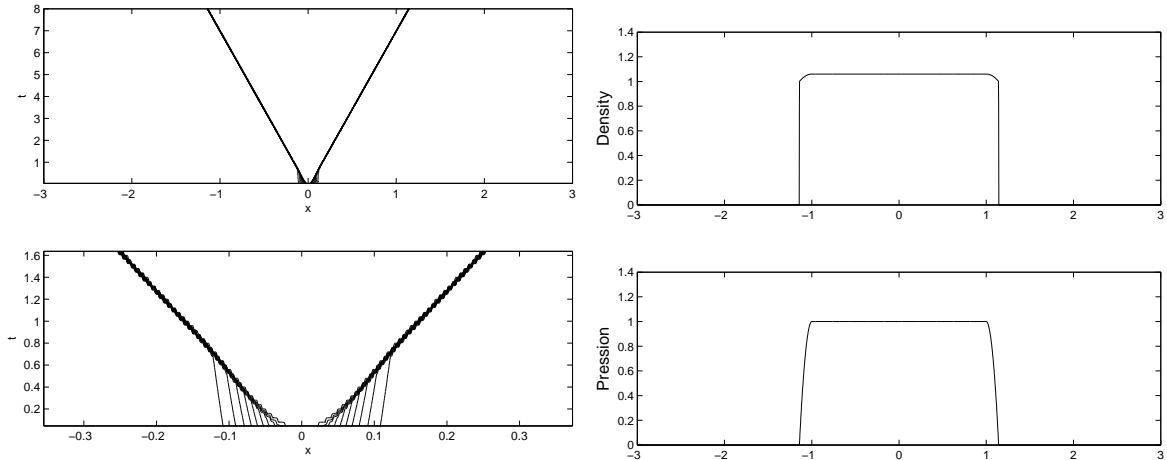


Figure 2: The traveling wave solution for $C_z = 0$, $\epsilon = 0$. The parameters are chosen as in (31). Left: the solution isolines; horizontal axis is x , vertical axis is time. The bottom subplot is the zoom in of the top subplot. Right: The traveling front at $T = 8$ (top: population density; bottom: pressure).

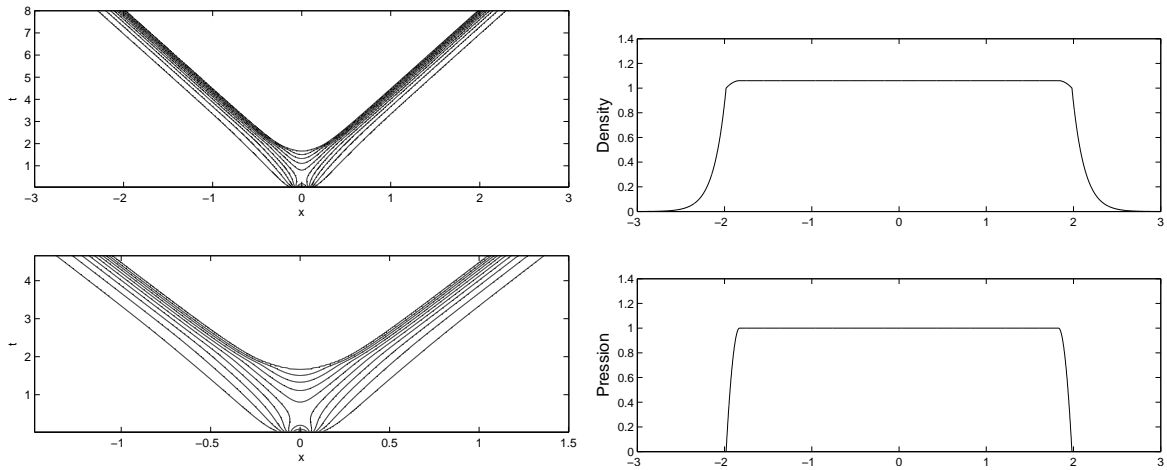


Figure 3: As Figure 2 with $C_z = 0$, $\epsilon = 0.02$.

C_p	C_S	ϵ	$\sqrt{2C_p C_S} + \frac{\epsilon}{\sqrt{2C_p C_S}}$	$2\sqrt{\epsilon}$	σ^*
0.57	0.001	0.001	0.0634	0.0632	0.0615
0.57	0.01	0.001	0.1161	0.0632	0.1155
1	0.01	0.001	0.1485	0.0632	0.1472
1	0.01	0.01	0.2121	0.200	0.2113
1	0.01	0.1	0.8485	0.632	0.5946
1	0.01	1	7.2125	2.000	1.9069

Table 1: Numerical values for the traveling speed σ^* with different parameters for $C_\nu = 17.114$ obtained by solving the evolution equation. We observe that the numerical speeds are close to $\sqrt{2C_p C_S} + \frac{\epsilon}{\sqrt{2C_p C_S}}$ or $2\sqrt{\epsilon}$ as computed in formula (30). In the first four lines $\epsilon < 2C_p C_S$, while in the last two $\epsilon > 2C_p C_S$.

still with the equation of state (11). In the interval $\{\rho \geq 1\}$, multiplying (7) by $\Sigma'(\rho) = C_\nu/\rho$, we get

$$-\sigma \partial_x \Sigma - C_S \partial_x \Sigma \partial_x W - C_S C_\nu \partial_{xx} W = C_\nu H(C_p - \Sigma) + \epsilon \frac{C_\nu}{\rho} \partial_{xx} \rho, \quad \text{for } \rho \geq 1. \quad (33)$$

Here the situation is much more complicated and a new phenomena appears; we need to clarify the meaning of the discontinuous growth term when $\Sigma = C_p$, which occurs on an interval and is not well defined in the singular incompressible cells limit we study here (see (36) below). To do so, we use a linear smoothing of the Heaviside function H such that

$$H_\eta(u) = \min\left(1, \frac{1}{\eta}u\right), \quad \text{for } \eta \in (0, C_p). \quad (34)$$

There are no explicit or semi-explicit solutions for the traveling waves in general due to the non-local aspect of the field W , again we refer to [27] for a proof of existence in a related case. Thus we will consider the incompressible cells limit. First, we derive formally the limiting system by letting $C_\nu \rightarrow +\infty$. From the state equation, we have $1 \leq \rho \leq \rho_M \rightarrow 1$. Therefore, we need to distinguish two cases : $\rho = 1$ and $\rho < 1$. Formally when $\rho < 1$, we find $\Sigma = 0$ and system (32) reduces to

$$\begin{cases} -\sigma \partial_x \rho - C_S \partial_x \rho \partial_x W - C_S \rho \partial_{xx} W = \rho + \epsilon \partial_{xx} \rho, & \rho < 1, \\ -C_z \partial_{xx} W + W = 0. \end{cases} \quad (35)$$

On the interval where $\rho = 1$, as $C_\nu \rightarrow +\infty$ the function Σ is not defined in terms of ρ and is left unknown, the formal limit of (32) implies a coupled system on W and Σ ,

$$\begin{cases} -C_S \partial_{xx} W = H_\eta(C_p - \Sigma), & \rho = 1, \\ -C_z \partial_{xx} W + W = \Sigma. \end{cases} \quad (36)$$

Then the existence of traveling waves in the asymptotic case $C_\nu \rightarrow +\infty$ boils down to study the asymptotic system (35)-(36). As in Section 3, the structure of the problem invites us to distinguish between the two cases $\epsilon = 0$ and $\epsilon \neq 0$.

4.1 Case $\epsilon = 0$.

Existence of traveling wave in the limit $C_\nu \rightarrow +\infty$. In this case, we can establish the

Theorem 4.1 Assume $C_z \neq 0$, $\epsilon = 0$ and $C_S C_p > 2C_z$. Then there exists $\sigma^* > 0$ such that for all $\sigma \geq \sigma^*$, the asymptotic system (35)–(36) admits a nonnegative and non-increasing solution (ρ, Σ) . Furthermore, when $\eta \rightarrow 0$, we have $\sigma^* = \sqrt{2C_S C_p} - \sqrt{C_z}$ and the solution is given by

$$\Sigma(x) = \begin{cases} C_p, & x \leq 0, \\ -\frac{x^2}{2C_S} - \frac{x}{C_S} \sqrt{C_z} + C_p, & 0 < x \leq \sqrt{2C_S C_p} - 2\sqrt{C_z} =: x_0, \\ 0, & x > x_0. \end{cases} \quad (37)$$

Therefore, Σ has a jump from $\sqrt{\frac{2C_p C_z}{C_S}}$ to 0 at x_0 . The population density satisfies

$$\rho = 1, \quad \text{for } x < x_0,$$

$$\begin{cases} \rho = 0, & \text{for } x > x_0, \quad \text{when } \sigma = \sigma^*, \\ \rho = \left(\sigma - \sigma^* e^{-(x-x_0)/\sqrt{C_z}} \right)^{-1-\sqrt{C_z}/\sigma} e^{-(x-x_0)/\sigma}, & \text{for } x > x_0, \quad \text{when } \sigma > \sigma^*. \end{cases}$$

Proof. By the maximum principle in Lemma 2.1, and according to Definition 2.2, Σ is bounded by C_p and nonnegative. Therefore, thanks to elliptic regularity, $\partial_{xx} W$ is bounded and W and $\partial_x W$ are continuous. Following the idea in the proof of Theorem 3.1 or 3.5, we look for a nonnegative and non-increasing traveling wave defined on $\mathbb{R} = I_1 \cup I_2 \cup I_3$ which has the following form :

- On $I_1 = (-\infty, 0]$, we have $\Sigma \in [C_p - \eta, C_p]$ so that the growth term is given by $H_\eta(C_p - \Sigma) = \frac{1}{\eta}(C_p - \Sigma)$.
- On $I_2 = (0, x_0)$, we have $\Sigma \in (0, C_p - \eta)$, thus $H_\eta(C_p - \Sigma) = 1$ and $\rho = 1$.
- On $I_3 = [x_0, +\infty)$, we have $\rho < 1$ and $\Sigma = 0$.

On I_1 , we have $\rho = 1$ and we solve (36). This system writes

$$-C_S \partial_{xx} W = \frac{1}{\eta}(C_p - \Sigma), \quad -C_z \partial_{xx} W + W = \Sigma.$$

Eliminating Σ in this system gives

$$-(\eta C_S + C_z) \partial_{xx} W + W = C_p.$$

Together with the boundary conditions of W at $-\infty$, we have

$$W = C_p + A e^{x/\sqrt{\eta C_S + C_z}} \quad \text{and} \quad \Sigma = C_p + \frac{\eta C_S A}{\eta C_S + C_z} e^{x/\sqrt{\eta C_S + C_z}}$$

which is the bounded solution on $I_1 = (-\infty, 0]$. The constant A can be determined as follows. Since Σ depends continuously on ρ and $\rho = 1$ on $I_1 \cup I_2$, Σ is continuous at x_0 . Therefore, A is computed by fixing $\Sigma(0) = C_p - \eta$, which gives $A = -\eta - C_z/C_S$.

On I_2 , we still have $\rho = 1$ and system (36) writes

$$-C_S \partial_{xx} W = 1, \quad -C_z \partial_{xx} W + W = \Sigma.$$

At the interface $x = 0$, W and $\partial_x W$ are continuous and given by their values on I_1 , then we can solve the first equation that gives

$$W(x) = -\frac{x^2}{2C_S} - \frac{x}{C_S} \sqrt{\eta C_S + C_z} + C_p - \eta - \frac{C_z}{C_S}. \quad (38)$$

Injecting this expression in the second equation implies

$$\Sigma(x) = -\frac{x^2}{2C_S} - \frac{x}{C_S} \sqrt{\eta C_S + C_z} + C_p - \eta.$$

On I_3 , since $\rho < 1$ we have to solve (35) with $\epsilon = 0$. The second equation in (35) can be solved easily and the only solution which is bounded on $(x_0, +\infty)$ is

$$W(x) = W(x_0)e^{-(x-x_0)/\sqrt{C_z}}. \quad (39)$$

We fix the value of x_0 by using the continuity of W and the derivative of W at x_0 . From (39), we have $-\frac{W(x_0)}{\sqrt{C_z}} = \partial_x W(x_0)$. This equality rewrites, from (38),

$$\frac{1}{\sqrt{C_z}} \left(\frac{x_0^2}{2C_S} + \frac{x_0}{C_S} \sqrt{\eta C_S + C_z} - C_p + \eta + \frac{C_z}{C_S} \right) = -\frac{x_0}{C_S} - \frac{1}{C_S} \sqrt{\eta C_S + C_z}.$$

This is a second order equation for x_0 whose only nonnegative solution (for η small enough) is

$$x_0 = \sqrt{2C_p C_S - \eta C_S} - \sqrt{C_z} - \sqrt{C_z + \eta C_S}. \quad (40)$$

Now we determine the expression for ρ on I_3 . The jump condition of (35) at x_0 in the case $\epsilon = 0$ writes : $\sigma[\rho]_{x_0} + C_S[\rho\partial_x W]_{x_0} = 0$. The continuity of $\partial_x W$ implies

$$[\rho]_{x_0} = 0, \quad \text{or} \quad \sigma = \sigma^* := -C_S \partial_x W(x_0) = x_0 + \sqrt{\eta C_S + C_z} = \sqrt{2C_p C_S - \eta C_S} - \sqrt{C_z}.$$

From the expression (39), the first equation in (35) with $\epsilon = 0$ gives

$$\left(\sigma - \sigma^* e^{-(x-x_0)/\sqrt{C_z}} \right) \partial_x \rho + \left(1 + \frac{\sigma^*}{\sqrt{C_z}} e^{-(x-x_0)/\sqrt{C_z}} \right) \rho = 0. \quad (41)$$

Looking for a non-increasing and nonnegative ρ implies that we should have $\sigma \geq \sigma^*$. After straightforward computation, we get that

$$\partial_x \rho = -\partial_x \left(\frac{x-x_0}{\sigma} + \left(1 + \frac{\sqrt{C_z}}{\sigma} \right) \ln \left(\sigma - \sigma^* e^{-(x-x_0)/\sqrt{C_z}} \right) \right) \rho. \quad (42)$$

If $[\rho]_{x_0} = 0$ and $\sigma > \sigma^*$, the Cauchy problem (42) with $\rho(x_0) = 1$ admits a unique solution which is given by

$$\rho(x) = \left(\sigma - \sigma^* e^{-(x-x_0)/\sqrt{C_z}} \right)^{-1-\sqrt{C_z}/\sigma} e^{-(x-x_0)/\sigma}.$$

When $\sigma = \sigma^*$, the factor of ρ on the right hand side of (42) has a singularity at $x = x_0$. Therefore the only solution which does not blow up in $x = x_0$ is $\rho = 0$. \square

Remark 4.2 When $\sqrt{2C_p C_S} < 2\sqrt{C_z}$, Σ becomes a step function with a jump from C_p to 0 at the point x_0 . The corresponding traveling speed is $\sigma = -C_S \partial_x W(x_0) = \frac{C_p C_S}{2\sqrt{C_z}}$ with

$$W(x) = \begin{cases} \frac{C_p}{2} e^{-\frac{1}{\sqrt{C_z}}(x-x_0)} & x > x_0, \\ C_p - \frac{C_p}{2} e^{\frac{1}{\sqrt{C_z}}(x-x_0)} & x < x_0. \end{cases}$$

The calculations are similar but simpler than in Lemma 4.1.

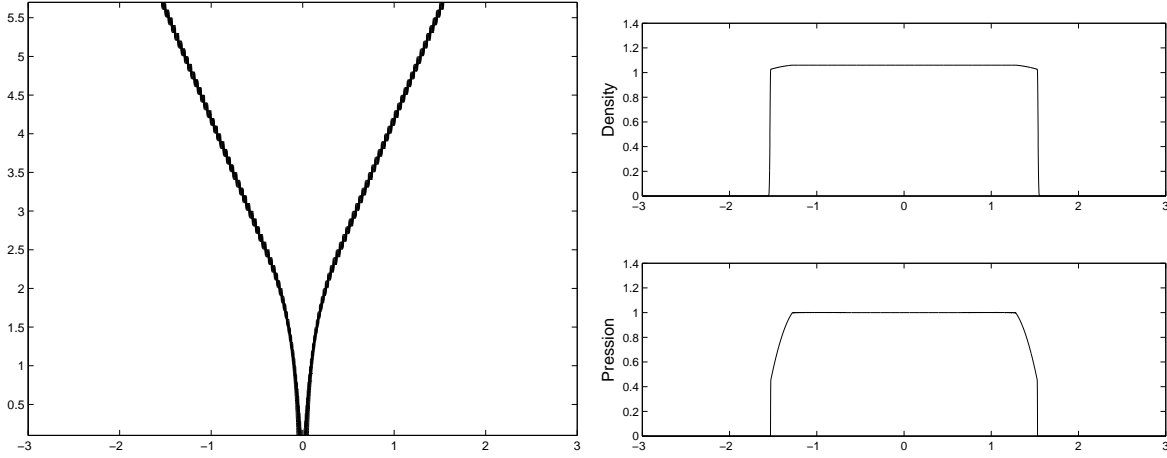


Figure 4: Numerical results when $C_p = 1$, $C_S = 0.1$, $C_\nu = 17.114$, $C_z = 0.01$ and $\epsilon = 0$, Left: the isolines of the traveling front with respect to time. Right: the front shapes of the density and pressure.

Remark 4.3 (Comparison with the case $C_z = 0$.) *In the asymptotic $\eta \rightarrow 0$, and when $C_z \rightarrow 0$, the expression for σ^* in Theorem 4.1 converges to that obtained for $C_z = 0$. However, we notice that, contrary to the case $C_z = 0$, the growth term does not vanish on I_1 whereas $\Sigma = C_p$. In fact, if the growth term was zero on I_1 , then since $\Sigma = C_p$, we would have $\partial_x \Sigma = 0$ and equation (33) gives*

$$-C_S C_\nu \partial_{xx} W = 0.$$

Thus $\partial_{xx} W = 0$ and $W = \Sigma$ on I_1 which can not hold true. That is why we cannot use the Heaviside function in the growth term when $\Sigma = C_p$ and the linear approximation in (34) allows us to make explicit calculations.

Numerical results. We present some numerical simulations of the full model (3) with growth term $\Phi = \rho H(C_p - \Sigma(\rho))$ and $\epsilon = 0$. As in the previous section, we consider a computational domain $\Omega = [-L, L]$ discretized by a uniform mesh and use Neumann boundary conditions. System (3) is now a coupling of a transport equation for ρ and an elliptic equation for W . We use following schemes

- The centered three point finite difference method is used to discretize the equation for W .
- A splitting method is implemented to update ρ . Firstly we use a first order upwind discretization of the term $-C_S \partial_x(\rho \partial_x W)$ (i.e. without right hand side), secondly we solve the growth term $\partial_t \rho = \rho H(C_p - \Sigma(\rho))$ with an explicit Euler scheme.

As before, starting from a Gaussian at the middle of the computational domain, Figure 4 shows the numerical traveling wave solutions for $C_z = 0.01$ and $\epsilon = 0$. We can observe that, at the traveling front, ρ has a jump from 1 to 0 and Σ has a layer and then jumps to zero. These observations are in accordance with our analytical results, in particular with (37) for Σ .

When $C_z = 0.4$, the relation $C_S C_p > 2C_z$ is no longer satisfied. However, we can perform numerical simulations and the results are presented in Figure 5. The proof of Theorem 4.1 shows that we can not have a traveling wave which satisfies the continuity relation for W and $\partial_x W$ at the point x_0 . In fact, we notice in Figure 5 that the pressure Σ seems to have a jump directly from 1 to 0 at the front position, which is in accordance to Remark 4.2.

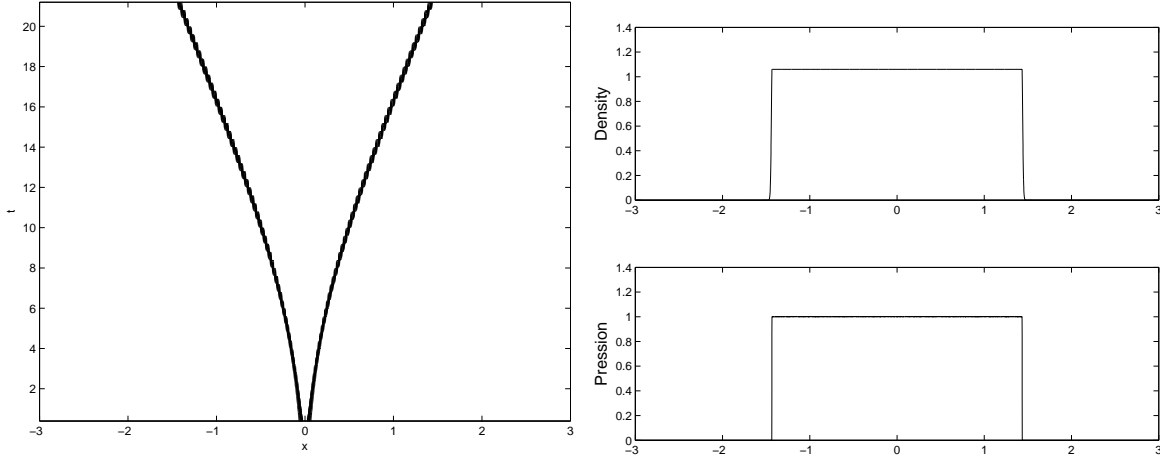


Figure 5: As in Figure 4 but violate the condition $C_S C_p > 2C_z$ using $C_p = 1$, $C_S = 0.1$, $C_\nu = 17.114$, $C_z = 0.4$ and $\epsilon = 0$.

With different choices of parameters, the numerical values for the traveling velocities σ and the front jumps of Σ at x_0 are given in Table 2, where we can verify the analytical formula in Theorem 4.1.

C_p	C_S	C_z	$\sqrt{2C_p C_S} - \sqrt{C_z}$	$\frac{C_p C_S}{2\sqrt{C_z}}$	σ^*	$\sqrt{\frac{2C_p C_z}{C_S}}$	$\Sigma(x_0)$
0.57	1	0.1	0.7515	0.9012	0.7616	0.3376	0.3342
0.57	1	0.01	0.9677	2.8500	0.9686	0.1068	0.1052
0.57	0.1	0.01	0.2376	0.2850	0.2438	0.3376	0.3362
1	0.1	0.01	0.3472	0.500	0.3507	0.4472	0.4129
1	0.1	0.0	0.4472	-	0.4424	0	0

Table 2: The traveling speed σ^* for different parameter values satisfying $2C_z < C_p C_S$. The numerical speeds are close to $\sqrt{2C_p C_S} - \sqrt{C_z}$ and the jump of Σ is not far from $\sqrt{\frac{2C_p C_z}{C_S}}$ as calculated in Theorem 4.1.

4.2 Case $\epsilon \neq 0$.

Existence of traveling waves. The case with diffusion such that $\epsilon \neq 0$, can be handled with the same method as above; we have

Theorem 4.4 *Assume $\epsilon \neq 0$, $C_z \neq 0$ and $C_S C_p > 2C_z$. Then there exists $\sigma^* > 0$ such that for all $\sigma \geq \sigma^*$, the asymptotic model (35)–(36) admits a nonnegative and non-increasing solution (ρ, Σ) . As $\eta \rightarrow 0$, the following bound on the minimal speed holds*

$$\max\{2\sqrt{\epsilon}, \sqrt{2C_S C_p} - \sqrt{C_z}\} \leq \sigma^* \leq (\sqrt{2C_S C_p} - \sqrt{C_z}) + 2\sqrt{\epsilon \sqrt{\frac{2C_S C_p}{C_z}}},$$

The solution is given by

$$\Sigma(x) = \begin{cases} C_p, & x \leq 0, \\ -\frac{x^2}{2C_S} - \frac{x}{C_S}\sqrt{C_z} + C_p, & 0 < x \leq \sqrt{2C_S C_p} - 2\sqrt{C_z}, \\ 0, & x > \sqrt{2C_S C_p} - 2\sqrt{C_z}. \end{cases} \quad (43)$$

The cell density ρ is a positive, non-increasing $C^1(\mathbb{R})$ function such that

$$\rho = 1, \quad \text{for } x < \sqrt{2C_S C_p} - 2\sqrt{C_z}; \quad \text{and } \rho < 1, \quad \text{for } x > \sqrt{2C_S C_p} - 2\sqrt{C_z}.$$

Proof. As above W and $\partial_x W$ are continuous on \mathbb{R} . Moreover, due to the diffusion term, ρ is continuous. Using the same decomposition $\mathbb{R} = I_1 \cup I_2 \cup I_3$ as before, we notice that on $I_1 \cup I_2$ the problem is independent of ϵ . Thus we have the same conclusion as in Theorem 4.1.

- On I_1 , we have $\rho = 1$, $\Sigma = C_p - \eta e^{x/\sqrt{\eta C_S + C_z}}$ and $W = C_p - (\eta + \frac{C_z}{C_S})e^{x/\sqrt{\eta C_S + C_z}}$.
- On I_2 , we have $\rho = 1$, $\Sigma = C_p - \eta - \frac{x}{C_S}\sqrt{\eta C_S + C_z} - \frac{x^2}{2C_S}$ and $W = C_p - \eta - \frac{C_z}{C_S} - \frac{x}{C_S}\sqrt{\eta C_S + C_z} - \frac{x^2}{2C_S}$.
- On I_3 , still from the second equation of (35) and the continuity of W and $\partial_x W$ we have

$$\begin{cases} W(x) = \frac{\sqrt{C_z}}{C_S}(\sqrt{C_z + \eta C_S} + x_0)e^{-(x-x_0)/\sqrt{C_z}}, \\ x_0 = \sqrt{2C_S C_p - \eta C_S} - \sqrt{C_z} - \sqrt{C_z + \eta C_S}. \end{cases} \quad (44)$$

The jump condition at x_0 for the first equation of (35) is

$$-\sigma[\rho]_{x_0} - C_S[\rho \partial_x W]_{x_0} = \epsilon[\partial_x \rho]_{x_0},$$

which implies $[\partial_x \rho]_{x_0} = 0$ thanks to the continuity of ρ and $\partial_x W$. Then, from (35), when $\rho < 1$, the density satisfies

$$\epsilon \partial_{xx} \rho + \left(\sigma - \frac{C_S}{\sqrt{C_z}} W \right) \partial_x \rho + \left(1 + \frac{C_S}{C_z} W \right) \rho = 0, \quad (45)$$

where W is as in (44). This equation is completed with the boundary conditions

$$\rho(x_0) = 1 \quad \text{and} \quad \partial_x \rho(x_0) = 0. \quad (46)$$

The Cauchy problem (45)–(46) admits a unique solution. Moreover, at the point x_0 , we deduce from (45) that

$$\epsilon \partial_{xx} \rho(x_0) = -1 - \frac{C_S}{C_z} W(x_0) < 0.$$

Therefore $\partial_x \rho$ is decreasing in the vicinity of x_0 . We deduce that $\partial_x \rho \leq 0$ for $x \geq x_0$ in the vicinity of x_0 . Then if ρ does not have a minimum on $(x_0, +\infty)$, it is a non-increasing function which necessarily tends to 0 at infinity from (45). If ρ admits a minimum at the point $x_m > x_0$, then we have $\partial_{xx} \rho(x_m) > 0$ and $\partial_x \rho(x_m) = 0$. We deduce from (45) that

$$\rho(x_m) \left(1 + \frac{C_S}{C_z} W(x_m) \right) = -\epsilon \partial_{xx} \rho(x_m) < 0.$$

We conclude that $\rho(x_m) < 0$. Thus there exists a point x_c such that $\rho(x_c) = 0$. Then on $[x_0, x_c)$, we have $\rho > 0$ and non-increasing. The question is then to know whether there exists values of σ for which $x_c = +\infty$. In order to do so, we will compare ρ with $\tilde{\rho}$ that satisfies

$$\epsilon \partial_{xx} \tilde{\rho} + \left(\sigma - \frac{C_S}{\sqrt{C_z}} K \right) \partial_x \tilde{\rho} + \left(1 + \frac{C_S}{C_z} K \right) \tilde{\rho} = 0, \quad x \in (x_0, +\infty) \quad (47)$$

with the boundary conditions

$$\tilde{\rho}(x_0) = 1, \quad \partial_x \tilde{\rho}(x_0) = 0. \quad (48)$$

Here K is a given constant which will be defined later.

Lower bound on σ^* : Integrating (45) from x_0 to $+\infty$, and using $\partial_x W = -\frac{W}{\sqrt{C_z}}$ and the boundary conditions in (46), we have

$$\sigma = \sqrt{C_z + \eta C_S} + x_0 + \int_{x_0}^{+\infty} \rho(x) dx.$$

We deduce that if we had a nonnegative solution ρ , then

$$\sigma \geq \sqrt{C_z + \eta C_S} + x_0 = \sqrt{2C_S C_p - \eta C_s} - \sqrt{C_z}. \quad (49)$$

Moreover, from (45), we have

$$\epsilon \partial_{xx} \rho + \sigma \partial_x \rho + \rho = \frac{C_S}{\sqrt{C_z}} W \partial_x \rho - \frac{C_S}{C_z} W \rho \leq 0.$$

Using the second assertion of Lemma 4.5, we can compare ρ with $\tilde{\rho}$ that is the solution of (47)–(48) with $K = 0$. We deduce that $\rho \leq \tilde{\rho}$. Since when $\sigma < 2\sqrt{\epsilon}$, $\tilde{\rho}$ takes negative values on I_3 . Thus, ρ is no longer nonnegative, which is a contradiction. Therefore,

$$\sigma \geq 2\sqrt{\epsilon}. \quad (50)$$

Upper bound on σ^* : We use the bound $W \leq W(x_0)$ to get

$$\epsilon \partial_{xx} \rho + \left(\sigma - \frac{C_S}{\sqrt{C_z}} W(x_0) \right) \partial_x \rho + \left(1 + \frac{C_S}{C_z} W(x_0) \right) \rho \geq 0. \quad (51)$$

Using assertion 1 of Lemma 4.5, we deduce that ρ is positive on I_3 provided

$$\sigma \geq \sqrt{2C_S C_p - \eta C_s} - \sqrt{C_z} + 2\sqrt{\epsilon \sqrt{\frac{2C_S C_p}{C_z}}}. \quad (52)$$

Thus for all σ satisfying (52), there exists a non-increasing and nonnegative solution ρ of (45)–(46).

However, the bound (52) is not satisfactory for small C_z . This is mainly due to the fact that the bound $W(x) \leq W(x_0)$ on I_3 is not sharp when C_z is small. We can improve this bound by using the remark that for any $x_z > x_0$, we have $W(x) \leq K := W(x_z)$. Let us define $x_z = x_0 + \sqrt{C_z} \xi(\sqrt{C_z})$ with a continuous function $\xi : (0, +\infty) \rightarrow (0, +\infty)$ such that $\lim_{x \rightarrow 0} x \xi(x) = 0$. Let us call $\hat{\rho}$ a solution of (47) on $(x_z, +\infty)$ with $K = W(x_z)$ and boundary conditions $\hat{\rho}(x_z) = \rho(x_z) > 0$ and $\partial_x \hat{\rho}(x_z) = \partial_x \rho(x_z) \leq 0$. Using assertion 1 of Lemma 4.5, we deduce that $\rho \geq \hat{\rho}$ and $\hat{\rho}$ is positive provided

$$\sigma \geq \frac{C_S}{\sqrt{C_z}} W(x_z) + 2\sqrt{\epsilon \left(1 + \frac{C_S}{C_z} W(x_z) \right)} \quad (53)$$

and

$$\alpha + \sqrt{\alpha^2 - 4\beta} \geq -2\partial_x \rho(x_z)/\rho(x_z), \quad (54)$$

where $\epsilon\alpha = \sigma - C_S W(x_z)/\sqrt{C_z}$ and $\epsilon\beta = 1 + C_S W(x_z)/C_z$. When $x_z \rightarrow x_0$, we have $\partial_x \rho(x_z) \rightarrow 0$, whereas $\alpha > 2/\sqrt{\epsilon}$ from (53). Thus for $\sqrt{C_z}$ small enough, (54) is satisfied provided (53) is satisfied, i.e.

$$\sigma \geq (\sqrt{2C_S C_p - \eta C_S} - \sqrt{C_z})e^{-\xi(\sqrt{C_z})} + 2\sqrt{\epsilon} \sqrt{1 + \left(\sqrt{\frac{2C_S C_p - \eta C_S}{C_z}} - 1 \right) e^{-\xi(\sqrt{C_z})}}. \quad (55)$$

Therefore, choosing the function ξ such that $\lim_{x \rightarrow 0} e^{-\xi(x)}/x = 0$ we deduce that when $C_z \rightarrow 0$, (55) becomes $\sigma \geq 2\sqrt{\epsilon}$. One possible choice is $\xi(x) = \ln x^2$. \square

The proof of Theorem 4.4 uses the

Lemma 4.5 *Let α, β, a be positive and $b \leq 0$. For $g \in C(\mathbb{R}_+)$, let f and \tilde{f} be the solutions to the Cauchy problems on \mathbb{R}_+ :*

$$f'' + \alpha f' + \beta f = g, \quad f(0) = a, \quad f'(0) = b. \quad (56)$$

$$\tilde{f}'' + \alpha \tilde{f}' + \beta \tilde{f} = 0, \quad \tilde{f}(0) = a, \quad \tilde{f}'(0) = b. \quad (57)$$

Then we have

1. Assume $g \geq 0$ on \mathbb{R}^+ . If $\alpha^2 \geq 4\beta$ and $\alpha + \sqrt{\alpha^2 - 4\beta} \geq -2b/a$, then $f(x) \geq \tilde{f}(x) > 0$ for $x \in \mathbb{R}_+$. Else, there exists $x_c > 0$ such that $\tilde{f}(x_c) = 0$ and $\tilde{f} \geq 0$ on $[0, x_c]$. Moreover, if $\alpha^2 < 4\beta$, we have $f(x) \geq \tilde{f}(x)$ for $x \in [0, 2\pi/\sqrt{4\beta - \alpha^2}]$; if $\alpha^2 \geq 4\beta$ and $\alpha + \sqrt{\alpha^2 - 4\beta} < -2b/a$, we have $f(x) \geq \tilde{f}(x)$ for $x \in [0, x_c]$.

2. Assume $g \leq 0$ on \mathbb{R}^+ . If $\alpha^2 \geq 4\beta$ then $f(x) \leq \tilde{f}(x)$ for $x \geq 0$. If moreover $\alpha + \sqrt{\alpha^2 - 4\beta} < -2b/a$, then f takes negative values on \mathbb{R}_+ . If $\alpha^2 < 4\beta$, then we have $f(x) \leq \tilde{f}(x)$ for $x \in [0, 2\pi/\sqrt{4\beta - \alpha^2}]$ and f takes negative values on $[0, 2\pi/\sqrt{4\beta - \alpha^2}]$.

Proof. Denote by r_1 and r_2 the roots of the characteristic equation $r^2 + \alpha r + \beta = 0$. Then, if $r_1 \neq r_2$, by solving (57) and (56), we have

$$\begin{aligned} \tilde{f}(x) &= \frac{r_2 a - b}{r_2 - r_1} e^{r_1 x} + \frac{r_1 a - b}{r_1 - r_2} e^{r_2 x}. \\ f(x) &= \tilde{f}(x) + \int_0^x g(y) \left(\frac{e^{r_1(x-y)}}{r_1 - r_2} + \frac{e^{r_2(x-y)}}{r_2 - r_1} \right) dy. \end{aligned} \quad (58)$$

First we assume that $g \geq 0$ on \mathbb{R}_+ . If $\alpha^2 > 4\beta$, then r_1 and r_2 are real negative. We deduce that

$$\frac{e^{r_1 x}}{r_1 - r_2} + \frac{e^{r_2 x}}{r_2 - r_1} > 0,$$

and then $f(x) > \tilde{f}(x)$ for $x \geq 0$. Moreover, \tilde{f} vanishes on \mathbb{R}_+ if and only if $\min\{r_1, r_2\} \geq b/a$.

If $\alpha^2 < 4\beta$, r_1 and r_2 are complex and $\bar{r}_1 = r_2$. We denote $r_1 = R - iI$ where $2R = -\alpha$ and $2I = \sqrt{4\beta - \alpha^2}$. We can rewrite then

$$\tilde{f}(x) = \left(\frac{R - b}{I} \sin(Ix) + a \cos(Ix) \right) e^{Rx}. \quad (59)$$

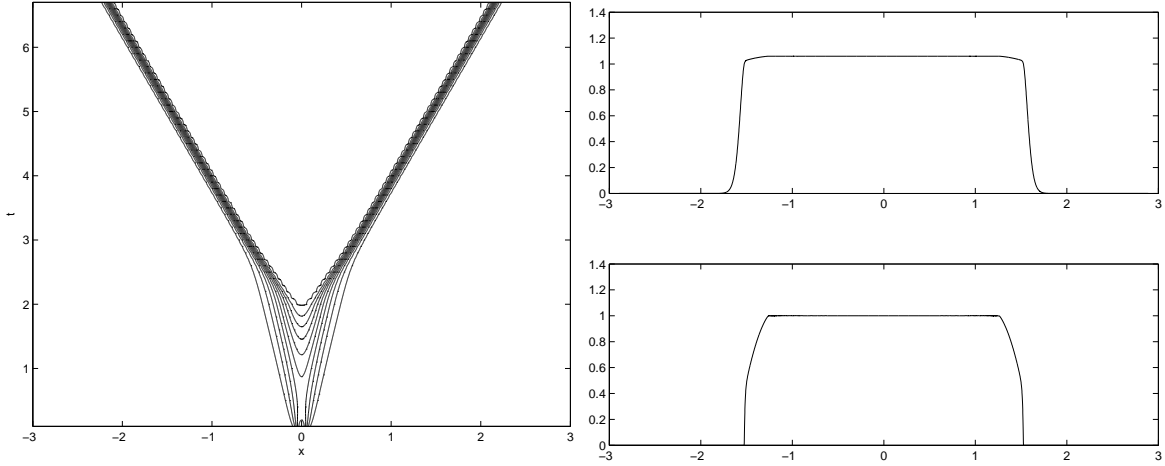


Figure 6: The numerical solution when $C_p = 1$, $C_S = 0.01$, $C_\nu = 17.114$, $C_z = 0.01$ and $\epsilon = 0.01$. Left: the isolines of the traveling front with respect to time. Right: the front shapes of the density and pressure.

We deduce that there exists x_c such that $\tilde{f}(x_c) = 0$ and $\tilde{f} \geq 0$ on $[0, x_c]$. Moreover,

$$\frac{e^{r_1 x}}{r_1 - r_2} + \frac{e^{r_2 x}}{r_2 - r_1} = \frac{e^{Rx}}{I} \sin(Ix) \geq 0, \quad \text{for } x \in [0, \pi/I]. \quad (60)$$

Thus $f(x) \geq \tilde{f}(x)$ if $x \in [0, \pi/I]$.

If $\alpha^2 = 4\beta$, we have $r_1 = r_2 = -\alpha/2$. By straightforward computation, we have $\tilde{f}(x) = ((b - ar_1)x + a)e^{rx}$, and

$$f(x) = \tilde{f}(x) + \int_0^x (x - y)e^{r_1(x-y)}g(y) dy. \quad (61)$$

For $g \geq 0$, we deduce $f \geq \tilde{f}$. This concludes the proof of the first point.

Let us consider that $g \leq 0$ on \mathbb{R}_+ . We deduce the first assertion from (58) and (61). If $\alpha^2 < 4\beta$, we deduce $f \leq \tilde{f}$ on $[0, \pi/I]$ from (58) and (60). And we have from (59) $\tilde{f}(\pi/I) = -ae^{\pi R/I} < 0$, thus f vanishes on $[0, \pi/I]$. \square

Numerical results. We perform numerical simulations of the full system (3) using the same algorithm as in section 4.1 and a centered finite difference scheme for the diffusion term $\epsilon \partial_{xx} \rho$.

We present in Figure 6 the numerical results still with parameters in (31) and $C_z = 0.01$, $\epsilon = 0.01$. Comparing Figure 4 and 6, we notice that the profile of ρ has a tail in the latter case.

Table 3 gives numerical values of the traveling velocity for different parameters. We illustrate numerically the bound on σ^* obtained in the proof of Theorem 4.4.

Acknowledgement

IC acknowledges support by the ANR grant PhysiCancer, DD acknowledges support by the ANR grant PhysiCancer and by the BMBF grant LungSys.

C_p	C_S	C_z	ϵ	$\sqrt{2C_p C_S} - \sqrt{C_z}$	$2\sqrt{\epsilon}$	σ^*
0.57	0.01	0.001	0.01	0.07515	0.20	0.197
0.57	0.1	0.01	0.01	0.2376	0.20	0.321
0.57	1	0.1	0.001	0.7514	0.0632	0.780
0.57	1	0.1	0.01	0.7514	0.2	0.828
0.57	1	0.1	0.1	0.7514	0.632	1.015
0.57	1	0.1	1	0.7514	2	1.974

Table 3: The traveling speed σ^* for equation (3) with different parameter values.

A Derivation of the cuboid state equation

Cells are modelled as cuboidal elastic bodies of dimensions at rest $L_0 \times l_0 \times h_0$ in x, y, z directions aligned in a row in x direction. At rest the lineic mass density of the row of cells, in contact but not deformed, is $\rho_0 = M_{cell}/L_0$. We consider the case where cells are confined in a tube of section $l_0 \times h_0$, where the only possible deformation is along the x axis. This situation can be tested in a direct in-vitro experiment. Moreover, this limit would be expected in case a tumor composed of elastic cells is sufficiently large such that for the ratio of the cell size L and the radius of curvature R , $L/R \ll 1$ holds, and the cell division is mainly oriented in radial direction as well as the cell-cell tangential friction is sufficiently small such that a fingering or buckling instability does not occur.

When cells are deformed, we assume that stress and deformation are uniformly distributed, and that the displacements are small. Let L be the size of the cells; the lineic mass density is $\rho = \rho_0 L_0/L$. For $\rho < \rho_0$, cells are not in contact and $\Sigma(\rho) = 0$; for $\rho \geq \rho_0$, a variation dL of the size L of the cell corresponds to an infinitesimal strain $du = \frac{dL}{L}$. Therefore, the strain for a cell of size L is $u = \ln(L/L_0)$. Assuming that a cell is a linear elastic body with Young modulus E and Poisson ratio ν , one finds that the component σ_{xx} of the stress tensor writes

$$\sigma_{xx} = -\frac{1-\nu}{(1-2\nu)(1+\nu)} E \ln(\rho/\rho_0).$$

The state equation is given by

$$\Sigma(\rho) = \begin{cases} 0 & \text{if } \rho \leq \rho_0 \\ \frac{1-\nu}{(1-2\nu)(1+\nu)} E \ln(\rho/\rho_0) & \text{otherwise.} \end{cases}$$

Here, $\Sigma(\rho) = -\sigma_{xx}$ is the pressure. Let $\bar{\rho} = \rho/\rho_0$, $\bar{\Sigma} = \Sigma/E_0$ and $\bar{E} = \frac{E}{E_0}$ be respectively the dimensionless density, pressure and Young modulus, with E_0 a reference Young modulus; then the state equation can be written:

$$\bar{\Sigma}(\bar{\rho}) = \begin{cases} 0 & \text{if } \bar{\rho} \leq 1 \\ C_\nu \ln(\bar{\rho}) & \text{otherwise.} \end{cases}$$

Where $C_\nu = \frac{\bar{E}(1-\nu)}{(1-2\nu)(1+\nu)}$. In the article, equations are written in dimensionless form, and the bars above dimensionless quantities are removed.

References

- [1] J. Adam, N. Bellomo, *A survey of models for tumor-immune system dynamics*, Birkhäuser, Boston, 1997.
- [2] D. Ambrosi, L. Preziosi, *On the closure of mass balance models for tumor growth*, Math. Models Methods Appl. Sci. **12** (2002), no. 5, 737–754.
- [3] A. Anderson, M.A.J. Chaplain, K. Rejniak, *Single-cell-based models in biology and medicine*, Birkhäuser, Basel, 2007.
- [4] R. Araujo, D. McElwain, *A history of the study of solid tumour growth: the contribution of mathematical models*, Bull Math Biol **66** (2004), 1039–1091.
- [5] N. Bellomo, N.K. Li., P.K. Maini, *On the foundations of cancer modelling: selected topics, speculations, and perspectives*. Math. Models Methods Appl. Sci. 4 (2008), 593–646.
- [6] N. Bellomo, L. Preziosi, *Modelling and mathematical problems related to tumor evolution and its interaction with the immune system*, Math. Comput. Model. **32** (2000) 413–452.
- [7] H. Berestycki, F. Hamel, *Reaction-Diffusion Equations and Propagation Phenomena*, Springer Verlag, New York (2012).
- [8] C.J.W. Breward, H.M. Byrne, C.E. Lewis, *The role of cell-cell interactions in a two-phase model for avascular tumour growth*, Journal of Mathematical Biology (2002), 45 (2) 125–152.
- [9] H. Byrne, D. Drasdo, *Individual-based and continuum models of growing cell populations: a comparison*, J. Math. Biol. **58** (2009) 657–687.
- [10] H.M. Byrne, J.R. King, D.L.S. McElwain and L. Preziosi, *A two-phase model of solid tumor growth*, Appl. Math. Lett. (2003) 16: 567–573.
- [11] H. Byrne, L. Preziosi, *Modelling solid tumour growth using the theory of mixtures*, Math. Med. Biol. (2003) 20: 341–366.
- [12] M.A.J. Chaplain, L. Graziano, L. Preziosi, *Mathematical modeling of the loss of tissue compression responsiveness and its role in solid tumor development*, Math. Med. Biol. (2006), 23, 197–229.
- [13] C. Chatelain, T. Balois, P. Ciarletta, M. Ben Amar, *Emergence of microstructural patterns in skin cancer: a phase separation analysis in a binary mixture*, New Journal of Physics **13** (2011) 115013+21.
- [14] I. Chedaddi, I.E. Vignon-Clementel, D. Hoehme, M. Tang, N. Vauchelet, B. Perthame, D. Drasdo., *On constructing discrete and continuous models for cell population growth with quantitatively equal dynamics*, Work in preparation.
- [15] P. Ciarletta, L. Foret, M. Ben Amar, *The radial growth phase of malignant melanoma: multi-phase modelling, numerical simulations and linear stability analysis*, J. R. Soc. Interface **8** (2011) no 56, 345–368.
- [16] T. Colin, D. Bresch, E. Grenier, B. Ribba, O. Saut, *Computational modeling of solid tumor growth: the avascular stage*, SIAM Journal of Scientific Computing (2010) 32 (4) 2321–2344.

- [17] V. Cristini, J. Lowengrub, Q. Nie, *Nonlinear simulations of tumor growth*, J. Math. Biol. **46** (2003), 191–224.
- [18] E. De Angelis, L. Preziosi, *Advection-diffusion models for solid tumour evolution in vivo and related free boundary problem*, Math. Models Methods Appl. Sci. **10** (2000), no. 3, 379–407.
- [19] D. Drasdo, *On selected individual-based approaches to the dynamics of multicellular systems*, In: Alt W, Chaplain M, Griebel M (eds) Multiscale modeling. Birkhauser, Basel, 2003.
- [20] L.C. Evans, *Partial Differential Equations*, Graduate Studies in Mathematics, vol. 19, American Mathematical Society (1998).
- [21] A. Friedman, *A hierarchy of cancer models and their mathematical challenges*, DCDS(B) **4**(1) (2004), 147–159.
- [22] M. Funaki, M. Mimura and A. Tsujikawa, *Traveling front solutions in a chemotaxis-growth model*, Interfaces and Free Boundaries, **8**, 223–245 (2006).
- [23] R.A. Gardner, *Existence of travelling wave solution of predator-prey systems via the connection index*, SIAM J. Appl. Math. **44** (1984), 56–76.
- [24] S. Hoehme, D. Drasdo, *A cell-based simulation software for multi-cellular systems*, Bioinformatics **26**(20) (2010) 2641–2642.
- [25] J.S. Lowengrub, H.B. Frieboes, F. Jin, Y.-L. Chuang, X. Li, P. Macklin, S.M. Wise, V. Cristini, *Nonlinear modelling of cancer: bridging the gap between cells and tumours*, Nonlinearity **23** (2010) R1–R91.
- [26] J. D. Murray, *Mathematical biology*, Springer-Verlag, 1989.
- [27] G. Nadin, B. Perthame, L. Ryzhik, *Traveling waves for the Keller-Segel system with Fisher birth terms*, Interfaces and Free Boundaries **10** (2008) 517–538.
- [28] B. Perthame, F. Quirós, J.-L. Vázquez *The Hele-Shaw asymptotics for mechanical models of tumor growth*, Work in preparation.
- [29] L. Preziosi, A. Tosin, *Multiphase modeling of tumor growth and extracellular matrix interaction: mathematical tools and applications*, J. Math. Biol. **58** (2009) 625–656.
- [30] M. Radszuweit, M. Block, J.G. Hengstler, E. Schöll, D. Drasdo, *Comparing the growth kinetics of cell populations in two and three dimensions*, Phys. Rev. E, **79**, (2009) 051907-1 - 12.
- [31] J. Ranft, M. Basan, J. Elgeti, J.-F. Joanny, J. Prost, F. Jülicher, *Fluidization of tissues by cell division and apoptosis*, PNAS **107** no 49 (2010) 20863–20868.
- [32] T. Roose, S. Chapman, P. Maini, *Mathematical models of avascular tumour growth: a review*, SIAM Rev. **49** 2, (2007) 179–208.
- [33] F. Sánchez-Garduño, P. K. Maini, *Travelling wave phenomena in some degenerate reaction-diffusion equations*, J. Differential Equations **117** (1995), no. 2, 281–319.
- [34] H. F. Weinberger, M. A. Lewis, B. Li, *Analysis of linear determinacy for spread in cooperative models*. J. Math. Biol. **45** (2002) 183–218.