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Analysis of a model of cell crawling migration*

Thomas Lepoutre [†] Nicolas Meunier [‡]

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Abstract

We introduce and study a model for motility of cells on substrate. The cell is 1d, inextensible and it contains a diffusive back-polarity marker, which satisfies a non-linear and non-local parabolic equation of Fokker-Planck type with attachment/detachment at the boundary. The idea behind the model is a quadratic nonlinear coupling: the marker is advected by the cell velocity, which is itself driven by a front-rear imbalance in marker. We show that it is of bistable type, provided that the coupling between the asymmetry of the marker and the cell velocity is sufficiently strong. In such a case we prove the non-linear stability of the largest steady state, for large initial data. In the weak coupling case we prove the convergence of the molecular concentration towards the Gaussian state.

keywords Cell polarisation, cell migration, global existence, asymptotic convergence.

AMS 35Q92; 92C17; 92B05.

1 Introduction

In this work we analyze a minimal model describing some aspects of cell motility. This model is based on a non-linear and non-local parabolic equation of Fokker-Planck type with attachment and detachment kinetic at the boundary. The Fokker-Planck equation without kinetic at the boundary, was introduced and studied in [13]. Here, from the mathematical viewpoint, the novelty is the attachment and detachment kinetic at the boundary.

The cell is modelled as the inextensible segment $[-1,1]$, with a boundary reduced to two points $\{-1,1\}$. For the description of the diffusive back-polarity marker, we distinguish between cytoplasmic content whose concentration is $c(t,x)$ and trapped molecules on the boundary whose concentrations are μ_{\pm} . We introduce the following function which describes cell marker imbalance

$$\delta\mu(t) = \mu_{-}(t) - \mu_{+}(t). \quad (1.1)$$

The model consists of the following equation

$$\begin{cases} \partial_t c(t,x) = \partial_{xx} c(t,x) + \partial_x((x + \eta\delta\mu(t))c(t,x)), & x \in (-1,1) \\ \frac{d}{dt}\mu_{-}(t) = c(t,-1) - \mu_{-}(t), \\ \frac{d}{dt}\mu_{+}(t) = c(t,1) - \mu_{+}(t), \end{cases} \quad (1.2)$$

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together with the flux condition at the boundary:

$$\begin{cases} \partial_x c(t, -1) + (-1 + \eta \delta \mu(t)) c(t, -1) = \frac{d}{dt} \mu_-(t), \\ \partial_x c(t, 1) + (1 + \eta \delta \mu(t)) c(t, 1) = -\frac{d}{dt} \mu_+(t). \end{cases} \quad (1.3)$$

The boundary condition (1.3) guarantees conservation of the total mass which is assumed to be 1, namely

$$\int_{-1}^1 c(t, x) dx + (\mu_-(t) + \mu_+(t)) = 1. \quad (1.4)$$

The cell velocity v is proportional to the front-rear marker imbalance

$$v(t) = -\gamma \delta \mu(t), \quad (1.5)$$

with $\gamma > 0$.

Briefly, the main assumptions that lead to (1.2) - (1.4) are the following: (i) the marker in the bulk can either freely diffuse or be actively transported by actin retrograd flow which is proportional to cell velocity, (ii) the cell velocity is itself driven by a front-rear marker imbalance $\delta \mu$ and (iii) actin depolymerisation leads to the x term in the drift. We refer to Section 2 for a detailed presentation of the model with biological motivations.

Several mathematical models have been proposed in the past decade to describe cell motility see [2, 3, 11, 13, 14, 24–26]. They incorporate many aspects of the mechanisms involved in migration. Although some of these models have been tested for their ability to fit quantitative data, they have not been quantitatively assessed for their ability to make accurate predictions with no additional free parameter. Here we will continue our analysis program of a model which was first introduced in [21] and then studied in [13]. Our objective is to derive, by rigorous analysis, the long time behavior of the solution to (1.2) - (1.4) and to go beyond the linear stability analysis performed in [21]. In order to bypass the lack of comparison principle, our method is based on a concentration-comparison principle that is obtained when equation (1.2) is integrated in space, see [19]. This principle allows to construct some remarkable sub/supersolutions and to perform a long-time analysis.

Before stating our results, let us give some comments. The dichotomy between concentration of the solution vs. convergence towards Gaussian profile presents some similarity with the classical Keller-Segel equation for chemotaxis [6]. However, there are two differences. Firstly, here the interaction goes through the values at the boundary, which makes the analysis more difficult. It is more singular, and furthermore it lacks symmetry properties. In particular as far as we know there is no free energy associated with (1.2) - (1.4). Secondly, the depolymerisation leads to the x term in the drift in equation (1.2). Nevertheless, we show here that the system inherits some structure from this analogy. This is quite remarkable as the system is genuinely non-linear.

Finally, let us mention that similar models involving a coupling between a one-dimensional PDE and a scalar boundary value appear in the modelling of NNLF models [7, 12] except that the derivative at the boundary is involved, among other differences.

Intuitively, the problem (1.2) - (1.4) is of bistable type, with a bifurcation for larger values of η . For small values of η and for any initial condition the density is expected to converge to the Gaussian profile G defined by

$$G(x) = \frac{e^{-\frac{x^2-1}{2}}}{2 + \int_{-1}^1 e^{-\frac{x^2-1}{2}} dx}, \quad (1.6)$$

and to follow the behaviour driven by the linear Fokker-Planck part. In such a case the cell velocity converges to zero. This corresponds to a "diffusive" cell migration phase with cell arrest. The coupling, described by the parameter η , is too weak to overcome the combined effects of friction and marker diffusion. For large values of η and for large enough initial data the concentration is expected to converge to the motile steady state G_α (to the right or to the left) defined by

$$G_\alpha(x) = \frac{\alpha}{1 - e^{-2\alpha\eta}} e^{-\frac{x^2-1}{2} - \alpha\eta(x+1)}, \quad (1.7)$$

where $\alpha > 0$ is defined by the mass constraint

$$M_\alpha := \frac{\alpha}{1 - e^{-2\alpha\eta}} \left(2 + \int_{-1}^1 e^{-\frac{x^2-1}{2} - \alpha\eta(x+1)} dx \right) - \alpha = 1. \quad (1.8)$$

This latter situation corresponds to a "persistent" migration phase, the coupling is strong and the cell reaches steady motility. In this work we are interested in making these informal statements rigorous.

Define η_0 by

$$\eta_0 = 1 + \frac{1}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} dx > 1, \quad (1.9)$$

and denote δ_{x_0} the Dirac measure in x_0 . The function C is the cumulated distribution function of $\mu_-(t)\delta_{-1} + c(t, x) dx$:

$$C(t, x) = \mu_-(t) + \int_0^x c(t, y) dy. \quad (1.10)$$

The functions C_G, C_{G_α} are respectively the cumulated distribution functions of $\frac{1}{2\eta_0}\delta_{-1} + G(x)dx$ and $\frac{\alpha}{1 - e^{-2\alpha\eta}}\delta_{-1} + G_\alpha(x)dx$.

Our first result states the convergence towards the Gaussian state for weak internal coupling. For strong internal coupling, it also gives sufficient conditions under which convergence towards the motile steady state holds.

Proposition 1. *Assume that $\int_{-1}^1 c^0 \log c^0 dx < +\infty$, then*

- for $\eta \leq \eta_0$ the solution to (1.2) - (1.4) converges to the unique steady state given by (1.6),
- for $\eta > \eta_0$, if $\liminf_{t \rightarrow \infty} \delta\mu(t) > 0$ (resp. $\limsup_{t \rightarrow \infty} \delta\mu(t) < 0$), then the solution (c, μ_-, μ_+) to (1.2) - (1.4) converges to G_α (resp. $G_{-\alpha}$).

Finally define the functions G^λ and C_λ by:

$$G^\lambda(x) = \frac{\int_{-1}^x e^{-\eta\lambda y + \frac{1-y^2}{2}} dy}{e^{\eta\lambda} + e^{-\eta\lambda} + \int_{-1}^1 e^{-\eta\lambda x + \frac{1-x^2}{2}} dx}, \quad (1.11)$$

and

$$C_\lambda(x) = \mu_-^\lambda + \int_{-1}^x G^\lambda(y) dy, \quad (1.12)$$

with

$$(\mu_-^\lambda, \mu_+^\lambda) = \frac{1}{e^{\eta\lambda} + e^{-\eta\lambda} + \int_{-1}^1 e^{-\eta\lambda x + \frac{1-x^2}{2}} dx} (e^{\eta\lambda}, e^{-\eta\lambda}). \quad (1.13)$$

For strong internal coupling, our second result provides some sufficient conditions on the initial data under which the convergence towards the motile state G_α (resp. $G_{-\alpha}$) occurs.

Proposition 2. *Assume that the initial data satisfy $\int_{-1}^1 c^0 \log c^0 dx < +\infty$ and that there exists $\lambda > 0$ such that*

$$C(0, x) \geq C_\lambda(x) \quad \forall x \in [-1, 1] \quad (\text{resp. } C(0, x) \leq C_{-\lambda}(x)).$$

Then the solution (c, μ_-, μ_+) to (1.2) - (1.4) converges to G_α (resp. $G_{-\alpha}$).

The article is organized as following. In Section 2 the origin of the model and its biophysical relevance are discussed in more details. In section 3 we provide a global existence theory for the above system. Section 4 is devoted to analytical investigations of the non-linear Fokker-Planck equation, namely the stationary state solutions. In section 5 we state a comparison principle. The quadratic structure of the problem is nontrivial and may lead to a bifurcation. In Section 6, in the case of small internal coupling, we prove cell arrest, and convergence towards a Gaussian profile, see proposition 1 and in the case of strong internal coupling together with large enough initial condition we prove convergence towards a motile state, see proposition 1 and proposition 2.

2 Further biological background

It is now well established that the displacement of cells is based on the appearance and maintenance of a functional asymmetry (polarity) between a "cell front" and a "cell rear". Biological markers of cell front-to-back polarity are e.g. the concentration and organization of actin filaments, levels of myo-II molecular motors. The polarization of motile cells can be induced by external gradient signals or appear spontaneously, by an intrinsic mechanism that produces and maintains directional persistence.

Here we represent the cell cytoskeleton by a layer of viscous fluid, surrounded by a rigid membrane. Following [5, 17], we model actin polymerization and depolymerization by adding active properties to the viscous fluid. Actin monomers are added to actin filaments by the consumption of biological fuel ATP. It is commonly observed that actin polymerization activators such as WASP proteins preferentially locate along the cell membrane. For this reason, we suppose that the fluid is polymerized at the membrane. Following the biological observations set in [21], the main ingredient of our model is the coupling between actin polymerization and a biological marker which is transported by actin flows. Its aggregation in a part of the membrane characterizes the cell rear, hence its polarisation. This marker could be an antagonist to polymerization-inducing molecules (Rac1, Cdc42), such as RhoA, Arpin, or even myosin II. Furthermore polymerization is balanced by depolymerization, which we assume to occur uniformly at a constant rate in the cell body, to ensure the renewal of resources for polymerization. Polymerization and depolymerization induce an inward flow which rubs on the substrate. This friction is responsible for the cell displacement.

More precisely, denote by ρ the actin concentration, by u its velocity with respect to the substrate and by $\Omega(t) = \{\rho(t, \cdot) > 0\}$ the region occupied by the cell. Considering a depolymerization rate k_d in the cell bulk, we can write

$$\partial_t \rho + \operatorname{div}(\rho u) = -k_d \rho \quad \text{in } \Omega(t).$$

To account for polymerization which consists in a local increase in actin concentration, we impose a jump on the cell membrane:

$$\rho = \rho_0 + \varepsilon k_p \quad \text{on } \partial\Omega(t),$$

where ε is a small parameter and ρ_0 is a constant.

To determine u , we write Stokes equation inside the cell. Indeed, in the limit of low Reynolds number, viscous forces dominate over inertial forces and the Navier-Stokes equation simplifies to the force balance principle:

$$-\operatorname{div} \sigma = f \quad \text{in } \Omega(t),$$

where $\sigma = \mu(\nabla u + {}^t\nabla u) - p \operatorname{Id}$ is the stress tensor with μ being the viscosity and f is the external force exerted on the actin filaments. We only take into account the friction of the polymers on the substrate that is $f = -\xi u$.

Following [8], we neglect viscosity arising from the polymer-polymer and polymer-solvent friction forces inside the cell and consider the limit $\mu \rightarrow 0$, hence we obtain:

$$\nabla p = -\xi u \quad \text{in } \Omega(t).$$

Furthermore, as it is classical, see [9] e.g., we assume that p is an osmotic pressure ensuring that the polymer density stays constant, namely we consider that p is the following function of ρ :

$$p = \frac{1}{\varepsilon}(\rho - \rho_0).$$

Therefore, we get the following problem for ρ :

$$\begin{cases} \partial_t \rho - \frac{1}{\xi} \operatorname{div}(\rho \nabla(\frac{\rho}{\varepsilon})) = -k_d \rho & \text{in } \Omega(t), \\ \rho = \rho_0 + \varepsilon k_p & \text{on } \partial\Omega(t). \end{cases}$$

Uniformly, taking the limit $\varepsilon \rightarrow 0$ of the previous model, it yields the Poisson problem:

$$\begin{cases} \operatorname{div} u = -\frac{1}{\xi} \Delta p = -k_d & \text{in } \Omega(t), \\ p = k_p & \text{on } \partial\Omega(t). \end{cases}$$

Finally, let us describe how the domain velocity arises from friction forces. Since the gel layer is at mechanical equilibrium, the cell moves as a consequence of the inside flow rubbing on the substrate, hence we will consider a moving domain. Friction forces occur at the microscopic scale, and mesoscopic tension forces also are at play. However, for the sake of simplicity, we will neglect this heterogeneity to consider a global friction coefficient γ , see [22] for more details about the adhesion force. Hence, for all $t > 0$ we write

$$v(t) = -\gamma \int_{\Omega(t)} u(t, x) dx.$$

Biological observations, see [21] e.g., show that nucleation of new filaments occurs at the cell membrane under the combined action of polymerization-inducing molecules. Therefore, we consider that k_p is a function of the concentration of antagonist to polymerization-inducing molecules trapped on the cell membrane and denoted by μ . This marker, whose concentration in the cell bulk is c , is assumed to diffuse and to

be transported by actin filaments. At the membrane, we prescribe a flux condition to ensure mass conservation (of c and μ). The corresponding problem writes

$$\begin{cases} \partial_t c + \operatorname{div}(uc - D\nabla c) = 0 & \text{in } \Omega(t), \\ (D\nabla c - cu) \cdot n = -\partial_t \mu & \text{on } \partial\Omega(t), \end{cases}$$

where n is the outward unit normal to the boundary.

In the one dimensional case where the cytoplasm of the cell is modelled by the interval $\Omega = (-1, 1)$, the model simply rewrites as (1.2) - (1.4) with $D = 1$, $k_p(\mu) = 2(1 - \mu)$, $k_d = 1$ and $\eta = \frac{1}{\xi}$.

3 Well-posedness of the coupled system (1.2) - (1.4)

In this part we prove the following result.

Proposition 3. *Assume that $\int_{-1}^1 c^0(x) \log c^0(x) dx < +\infty$ and that $\mu_-, \mu_+^0 \in [0, 1]$ are such that $\int_{-1}^1 c^0(x) dx + \mu_-^0 + \mu_+^0 = 1$. Then there exists a unique solution (c, μ_-, μ_+) to (1.2) - (1.4) for all time.*

Well-posedness of the Cauchy problem (1.2) - (1.4) relies on a fixed point theorem. We proceed into two steps. First, we obtain refined entropy estimates for the sole PDE problem, without the coupling. As such, we consider two given couples of functions $(\mu_-^1(t), \mu_+^1(t))$ and $(\mu_-^2(t), \mu_+^2(t))$, and we derive suitable contraction estimates on c_1, c_2 . We introduce the coupling in a second step.

3.1 An uncoupled PDE

Given the functions μ_-, μ_+ , we consider the solution c of the problem

$$\begin{cases} \partial_t c(t, x) - \partial_{xx} c(t, x) - \partial_x(v(t, x)c(t, x)) = 0, & x \in (-1, 1), \\ \partial_x c(t, 1) + v(t, 1)c(t, 1) = -(c(t, 1) - \mu_+(t)), \\ \partial_x c(t, -1) + v(t, -1)c(t, -1) = c(t, -1) - \mu_-(t), \\ c(0, x) = c^0(x), & x \in (-1, 1). \end{cases} \quad (3.14)$$

We start by a result concerning the sign of the solution to (3.14). For smooth v, μ the local existence is obtained by standard theory. Moreover, if $\mu_{\pm} \geq 0$ and $c^0 \geq 0$, the solution remains nonnegative. For instance, we can apply the Stampacchia argument and multiply the equation by $c_- = \min(c, 0)$, getting

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \|c^-(t)\|_{L^2}^2 &= -\|\partial_x c^-(t)\|_{L^2}^2 - \int_{-1}^1 \partial_x c^-(t, x) c^-(t, x) (x + v(t, x)) dx \\ &\quad - c^-(t, 1) (c(t, 1) - \mu_+(t)) - c^-(t, -1) (c(t, -1) - \mu_-(t)) \\ &\leq \frac{1}{4} \|v(t)\|_{L^\infty}^2 \|c^-(t)\|_{L^2}^2. \end{aligned}$$

As for $\mu_{\pm} \geq 0$, $c_-(t, \pm 1)(c(t, \pm 1) - \mu_{\pm}) = c(t, \pm 1)^2 - c_-(t, \pm 1)\mu_{\pm} \geq 0$. Using Gronwall's lemma and $\|c^{0-}\|_{L^2} = 0$, we deduce $\|c^-(t)\|_{L^2} = 0$ for all time $t \in [0, T]$.

Lemma 4. Assume that $c^0 > 0 \in L^2$ and $\mu_{\pm} \in C^0(\mathbb{R}_0)$ satisfy $1 \geq \mu_{\pm}(t) \geq \mu_{\pm}(0)e^{-t} > 0$. Assume v is $C^1(\mathbb{R}_+ \times [-1, 1])$. Then the (nonnegative) solution of (3.14) exists globally in $L_{loc}^{\infty}(\mathbb{R}_+, L \log L(-1, 1)) \cap L_{loc}^1(\mathbb{R}_+, W^{1,1}(-1, 1))$. Moreover, we have the estimate

$$\int_{-1}^1 c(t, x) dx \leq \int_{-1}^1 c^0(x) dx + 2t. \quad (3.15)$$

Proof. We start with a few simple estimates, since $\mu_+(t) + \mu_-(t) \leq 2$ for all $t \geq 0$, we have

$$\frac{d}{dt} \int_{-1}^1 c(t, x) dx = \mu_+(t) - c(t, 1) + \mu_-(t) - c(t, -1) \leq 2,$$

leading to (3.15).

First, using

$$\begin{aligned} & (c(t, x) - \mu(t)) \log c(t, x) - (1 - \mu(t)) \log \mu(t) \\ &= (c(t, x) - \mu(t)) \log \frac{c(t, x)}{\mu(t)} + (c(t, x) - 1) \log \mu(t), \end{aligned}$$

we deduce that for $\mu \leq 1$ and $c > 0$, the following inequality holds

$$(c(t, x) - \mu(t)) \log c(t, x) \geq (1 - \mu(t)) \log \mu(t).$$

We do not fully detail the global existence, only the key estimate

$$\begin{aligned} & \frac{d}{dt} \int_{-1}^1 (c(t, x) \log c(t, x) - c(t, x)) dx \\ &= -\log c(t, 1)(c(t, 1) - \mu_+(t)) - \log c(t, -1)(c(t, -1) - \mu_-(t)) \\ & \quad - \int_{-1}^1 c(t, x) \partial_x \log c(t, x) (\partial_x \log c(t, x) + v(t, x)) dx \\ &\leq -\log \mu_+(t)(1 - \mu_+(t)) - \log \mu_-(t)(1 - \mu_-(t)) \\ & \quad - \frac{1}{2} \int_{-1}^1 c(t, x) |\partial_x \log c(t, x)|^2 dx + \frac{1}{2} \int_{-1}^1 c(t, x) |v(t, x)|^2 dx, \\ &\leq -\log \mu_+^0 - \log \mu_-^0 + 2t \\ & \quad - \frac{1}{2} \int_{-1}^1 c(t, x) |\partial_x \log c(t, x)|^2 dx + \frac{\|v\|_{\infty}}{2} \left(\int_{-1}^1 c^0(x) dx + 2t \right). \end{aligned}$$

From this we easily infer an estimate of the form

$$\int_{-1}^1 c(t, x) |\log c(t, x)| dx \leq C(1 + t^2).$$

and also $\int_0^t \int_{-1}^1 c |\partial_x \log c|^2 dx ds \leq C(1 + t^2)$ and finally

$$\begin{aligned} \int_0^t \int_{-1}^1 |\partial_x c| dx ds &\leq \|\sqrt{c}\|_{L^2((0,t) \times (-1,1))} \|c |\partial_x \log c|\|_{L^2((0,t) \times (-1,1))} \\ &\leq C\sqrt{1+t^2} \cdot \sqrt{1+t^2} \leq C(1+t^2). \end{aligned}$$

□

In order to compare two solutions c_1 and c_2 associated with two inputs (μ_{\pm}^1, v^1) and (μ_{\pm}^2, v^2) , we introduce the Gajewski metric [16]:

$$d_G(c_1, c_2) = \int_{-1}^1 h(c_1) + h(c_2) - 2h\left(\frac{c_1 + c_2}{2}\right) dx,$$

where h is the convex function

$$h(a) = a \log a - a + 1. \quad (3.16)$$

We also define the function $\Delta_h(c_1, c_2)$ by

$$\Delta_h(c_1, c_2) = h(c_1) + h(c_2) - 2h\left(\frac{c_1 + c_2}{2}\right) dx \geq 0.$$

We start with a technical result.

Lemma 5. *The following inequalities hold*

$$\frac{1}{4} \frac{(b-a)^2}{a+b} \leq \frac{1}{4} \frac{(b-a)^2}{\max(a,b)} \leq \Delta_h(a, b) \leq \frac{1}{4} \frac{(b-a)^2}{\min(a,b)}, \quad (3.17)$$

and

$$d_G(c_1, c_2) \geq \frac{1}{4} \frac{\left(\int_{-1}^1 c_1 dx - \int_{-1}^1 c_2 dx\right)^2}{\int_{-1}^1 c_1 dx + \int_{-1}^1 c_2 dx}. \quad (3.18)$$

Proof. For all a, b , we have:

$$h(b) - h\left(\frac{a+b}{2}\right) = h'\left(\frac{a+b}{2}\right) \left(\frac{b-a}{2}\right) + \frac{1}{2} h''(c) \left(\frac{b-a}{2}\right)^2, \quad (3.19)$$

for some $c \in [a, b]$, and a similar estimate at point a . This yields inequalities (3.17).

The pointwise inequality turns into the following integral from which inequality (3.18) follows by Cauchy-Schwarz inequality:

$$d_G(c_1, c_2) \geq \frac{1}{4} \int_{-1}^1 \frac{(c_1 - c_2)^2}{c_1 + c_2} dx.$$

□

In the sequel, we use the index or exponent m for the midpoint

$$c_m = \frac{c_1 + c_2}{2}, \mu_+^m = \frac{\mu_1 + \mu_2}{2} \dots$$

Denoting $q_i = \frac{c_i}{c_m}$, we notice that $q_1 + q_2 = 2$ and thus $\partial_x q_1 = -\partial_x q_2$.

Lemma 6. *Let c_i the solution associated to (3.14) with (μ_-^i, μ_+^i) . Then the following inequality holds*

$$\begin{aligned} \frac{d}{dt} d_G(c_1, c_2) &\leq \Delta_h(\mu_-^1, \mu_-^2) + \Delta_h(\mu_+^1, \mu_+^2) - \Delta_h(c_1(1), c_2(1)) \\ &\quad - \Delta_h(c_1(-1), c_2(-1)) + \|v^1(t, \cdot) - v^2(t, \cdot)\|_{\infty}^2 \int_{-1}^1 \frac{c_1 + c_2}{2} dx \\ &\quad - \frac{3}{4} \left(\int_{-1}^1 c_1 |\partial_x \log q_1|^2 dx + \int_{-1}^1 c_2 |\partial_x \log q_2|^2 dx \right). \end{aligned} \quad (3.20)$$

Proof. We have

$$\begin{aligned} \frac{d}{dt}(d_G(c_1, c_2)) &= \int_{-1}^1 (\partial_t c_1 \log q_1 + \partial_t c_2 \log q_2) dx \\ &= - \sum_{i=1}^2 ((c_i(t, 1) - \mu_+^i) \log q_i(t, 1) + (c_i(t, -1) - \mu_-^i) \log q_i(t, -1)) \\ &\quad - \sum_{i=1}^2 \int_{-1}^1 (\partial_x c_i + v^i c_i) \partial_x \log q_i dx, \end{aligned}$$

which rewrites as

$$\begin{aligned} \frac{d}{dt} d_G(c_1, c_2) &= \sum_{i=1}^2 (\mu_+^i \log q_i(1) + \mu_-^i \log q_i(-1)) \\ &\quad - \Delta_h(c_1(1), c_2(1)) - \Delta_h(c_1(-1), c_2(-1)) \\ &\quad - \sum_{i=1}^2 \int_{-1}^1 \frac{c_1 + c_2}{2} (\partial_x \log c_i + v^i) \partial_x q_i dx. \end{aligned}$$

To bound the cross term involving μ_{\pm}^i and $c_i(\pm 1)$ in the first line, we notice that the function

$$\mu_1 \log q + \mu_2 \log(2 - q)$$

reaches a maximum for the critical value q^* satisfying

$$\frac{\mu_1}{q^*} = \frac{\mu_2}{2 - q^*}, \quad q^* = \frac{2\mu_1}{\mu_1 + \mu_2}.$$

Therefore, the first line is upper bounded by

$$\sum_{i=1}^2 \left(\mu_+^i \log \left(\frac{2\mu_+^i}{\mu_+^1 + \mu_+^2} \right) + \mu_-^i \log \left(\frac{2\mu_-^i}{\mu_-^1 + \mu_-^2} \right) \right) = \Delta_h(\mu_-^1, \mu_-^2) + \Delta_h(\mu_+^1, \mu_+^2).$$

We arrive at

$$\begin{aligned} \frac{d}{dt} d_G(c_1, c_2) &\leq \Delta_h(\mu_-^1, \mu_-^2) + \Delta_h(\mu_+^1, \mu_+^2) - \Delta_h(c_1(1), c_2(1)) - \Delta_h(c_1(-1), c_2(-1)) \\ &\quad - \sum_{i=1}^2 \int_{-1}^1 \frac{c_1 + c_2}{2} \partial_x q_i (\partial_x \log c_i + v^i) dx \\ &= \Delta_h(\mu_-^1, \mu_-^2) + \Delta_h(\mu_+^1, \mu_+^2) - \Delta_h(c_1(1), c_2(1)) - \Delta_h(c_1(-1), c_2(-1)) \\ &\quad - \int_{-1}^1 \frac{c_1 + c_2}{2} \partial_x q_1 \left(\partial_x \log \frac{c_1}{c_2} + v^1 - v^2 \right) dx. \end{aligned}$$

We recall that $\frac{c_1}{c_2} = \frac{q_1}{2 - q_1}$, so that

$$\partial_x \log \frac{c_1}{c_2} = \frac{2}{q_1(2 - q_1)} \partial_x q_1 = .$$

$$\frac{d}{dt} d_G(n_1, n_2) \leq \Delta_h(\mu_-^1, \mu_-^2) + \Delta_h(\mu_+^1, \mu_+^2) - \Delta_h(c_1(1), c_2(1)) - \Delta_h(c_1(-1), c_2(-1))$$

$$\begin{aligned}
& - \int_{-1}^1 \frac{c_1 + c_2}{q_1(2 - q_1)} |\partial_x q_1|^2 dx - \int_{-1}^1 \frac{c_1 + c_2}{2} (v^1 - v^2) \partial_x q_1 dx \\
& \leq \Delta_h(\mu_-^1, \mu_-^2) + \Delta_h(\mu_+^1, \mu_+^2) - \Delta_h(c_1(1), c_2(1)) - \Delta_h(c_1(-1), c_2(-1)) \\
& - \frac{1}{2} \int_{-1}^1 \frac{c_1 + c_2}{q_1(2 - q_1)} |\partial_x q_1|^2 dx \\
& + \|v^1(t, \cdot) - v^2(t, \cdot)\|_\infty \int_{-1}^1 \frac{c_1 + c_2}{2} \underbrace{q_1(2 - q_1)}_{\leq 1} dx
\end{aligned}$$

Using again the relationship $q_1 + q_2 = 2$ and $\partial_x q_1 = -\partial_x q_2$, we see that

$$\frac{2}{q_1(2 - q_1)} |\partial_x q_1|^2 = \frac{|\partial_x q_1|^2}{q_1} + \frac{|\partial_x q_1|^2}{2 - q_1} = q_1 |\partial_x \log q_1|^2 + q_2 |\partial_x \log q_2|^2.$$

Therefore,

$$\frac{c_1 + c_2}{q_1(2 - q_1)} |\partial_x q_1|^2 = c_1 |\partial_x \log q_1|^2 + c_2 |\partial_x \log q_2|^2.$$

and we end up with estimate (3.20). \square

3.2 The fixed point mapping

We now apply the previous estimates to a specific case. For a fixed $T > 0$, we define the space X by

$$\begin{aligned}
X = \{ & (\mu_-, \mu_+) \in C(0, T), \forall t \in (0, T) \mu_+^0 e^{-t} \leq \mu_+(t) \leq 1, \mu_-^0 e^{-t} \leq \mu_-(t) \leq 1, \\
& \mu_+(0) = \mu_+^0, \mu_-(0) = \mu_-^0 \}.
\end{aligned}$$

Taking $(\mu_-, \mu_+) \in X$, we solve (3.14) with $v(t, x) = x + \eta(\mu_-(t) - \mu_+(t))$. We define then

$$\nu_\pm(t) = \mu_\pm(0) + \int_0^t (c(s, \pm 1) - \mu_\pm(s)) ds,$$

the truncation function χ by

$$\chi(x) = \begin{cases} 0 & x \leq 0, \\ x & x \in]0, 1[, \\ 1 & x \geq 1, \end{cases}$$

and the mapping F by

$$\begin{cases} F & : X \mapsto X \\ & (\mu_+, \mu_-) \rightarrow (\chi(\nu_+), \chi(\nu_-)). \end{cases} \quad (3.21)$$

Denote F^n the function composed n times with itself, that is $F^n = F \circ F \circ \dots \circ F$.

In this part we prove the following result.

Proposition 7. *There holds*

$$\|F^n(\mu_+^1, \mu_-^1) - F^n(\mu_+^2, \mu_-^2)\|_X \leq \frac{(C(T)T)^n}{n!}.$$

Therefore F^n is a contraction once we take n large enough.

Proof. By construction, we have

$$\nu_{\pm}(t) = e^{-t} \mu_{\pm}^{\text{out}}(0) + \int_0^t e^{s-t} c(s, \pm 1) ds, \quad (3.22)$$

with the initial data satisfying

$$\nu_{-}(0) + \nu_{+}(0) = 1 - \int_{-1}^1 c^0(x) dx > 0.$$

Since we assume that the functions μ_{\pm}^i are continuous and take initial values such that $c^i(0, x), \mu_{\pm}^i(0)$ are the same for $i=1, 2$. In particular we have $d_G(c_1^0, c_2^0) = 0$. In addition we assume the following condition on the functions μ_{\pm}^i :

$$\mu_{\pm}^i(t) \geq \mu_{\pm}(0) e^{-t} > 0 \quad \text{and} \quad \mu_{+}^i(t) + \mu_{-}^i(t) \leq 2.$$

Using (3.17), we have

$$\Delta_h(\mu_{+}^1(s), \mu_{+}^2(s)) \leq \frac{e^s}{4\mu_{+}(0)} |\mu_{+}^1(s) - \mu_{+}^2(s)|^2.$$

Integrating estimate (3.20), we obtain

$$\begin{aligned} & \int_0^t (\Delta_h(c_1(s, 1), c_2(s, 1)) + \Delta_h(c_1(s, -1), c_2(s, -1))) ds \\ & \leq C(t) \int_0^t (|\mu_{+}^1(s) - \mu_{+}^2(s)|^2 + |\mu_{-}^1(s) - \mu_{-}^2(s)|^2) ds. \end{aligned}$$

Then, we can estimate

$$\begin{aligned} & \left(\int_0^t |c_1(s, 1) - c_2(s, 1)| ds \right)^2 \leq \int_0^t \frac{|c_1(s, 1) - c_2(s, 1)|^2}{c_1(s, 1) + c_2(s, 1)} ds \int_0^t (c_1(s, 1) + c_2(s, 1)) ds \\ & \leq 4 \int_0^t \Delta_h(c_1(s, 1), c_2(s, 1)) ds \left(2\mu_{+}(0) + \int_0^t \mu_{+}^1(s) + \mu_{+}^2(s) ds \right) \\ & \leq 8(1+t) \int_0^t \Delta_h(c_1(s, 1), c_2(s, 1)) ds, \end{aligned}$$

and similarly for $x = -1$. So that, finally, we have an estimate of the form

$$\begin{aligned} & \left(\int_0^t |c_1(s, 1) - c_2(s, 1)| ds \right)^2 + \left(\int_0^t |c_1(s, -1) - c_2(s, -1)| ds \right)^2 \\ & \leq C_2(t) \left(\int_0^t |\mu_{+}^1(s) - \mu_{+}^2(s)|^2 + |\mu_{-}^1(s) - \mu_{-}^2(s)|^2 ds \right). \end{aligned}$$

Using

$$\left(\int_0^t |\mu_{+}^1(s) - \mu_{+}^2(s)| ds \right)^2 \leq \left(\int_0^t |\mu_{+}^1(s) - \mu_{+}^2(s)|^2 ds \right) t$$

we deduce that

$$\left(\int_0^t |c_1(s, 1) - c_2(s, 1)| ds \right)^2 + \left(\int_0^t |c_1(s, -1) - c_2(s, -1)| ds \right)^2$$

$$\begin{aligned}
& + \left(\int_0^t |\mu_+^1(s) - \mu_+^2(s)| ds \right)^2 + \left(\int_0^t |\mu_-^1(s) - \mu_-^2(s)| ds \right)^2 \\
& \leq (C'(t) + t) \int_0^t (|\mu_+^1(s) - \mu_+^2(s)|^2 + |\mu_-^1(s) - \mu_-^2(s)|^2) ds.
\end{aligned}$$

We have

$$\begin{aligned}
& \left(\int_0^t |(c_1(s, 1) - c_2(s, 1)) - (\mu_+^1(s) - \mu_+^2(s))| ds \right)^2 \\
& + \left(\int_0^t |c_1(s, -1) - c_2(s, -1) - (\mu_-^1(s) - \mu_-^2(s))| ds \right)^2 \\
& \leq 2(C_2(t) + t) \left(\int_0^t |\mu_+^1(s) - \mu_+^2(s)|^2 + |\mu_-^1(s) - \mu_-^2(s)|^2 ds \right).
\end{aligned}$$

Finally, from the definitions and the fact that $\mu_{\pm}^{out,i}(0) = \mu_{\pm}^{in,i}(0) = \mu_{\pm}(0)$, we can write for $\mu_{\pm}(0)e^{-t} \leq \mu_{\pm}^{u,in} \leq 1$

$$\begin{aligned}
& (\nu_+^1(t) - \nu_+^2(t))^2 + (\nu_-^1(t) - \nu_-^2(t))^2 \\
& \leq C(t) \int_0^t (\mu_+^1(s) - \mu_+^2(s))^2 + (\mu_-^1(s) - \mu_-^2(s))^2 ds.
\end{aligned}$$

Using the truncation χ which is 1-Lipschitz,

$$\begin{aligned}
& (\chi(\nu_+^1(t)) - \chi(\nu_+^2(t)))^2 + (\chi(\nu_-^1(t)) - \chi(\nu_-^2(t)))^2 \\
& \leq C(T) \int_0^t (\mu_+^1(s) - \mu_+^2(s))^2 + (\mu_-^1(s) - \mu_-^2(s))^2 ds,
\end{aligned}$$

and with a classical iteration we obtain the result. □

4 Stationary solutions

In this section we compute the stationary states of the PDE (1.2) - (1.4) by setting $\partial_t c = 0$ and solving the resulting spatial ODE. We find that there exists a threshold value η_0 such that when $\eta > \eta_0$ the problem (1.2) - (1.4) admits non Gaussian stationary states that are steadily moving states while when $\eta \leq \eta_0$ it only admits the symmetric Gaussian stationary solution.

Proposition 8. *Let η_0 be defined by (1.9). Consider equations (1.2) - (1.4). The following alternative holds true:*

- for $0 \leq \eta \leq \eta_0$, the problem admits a unique symmetric Gaussian stationary solution \tilde{G} defined by (1.6).
- for $\eta > \eta_0$, there are three stationary solutions, the Gaussian profile, \tilde{G} , and two asymmetric profiles $\tilde{G}_{\pm\alpha}$ defined by (1.7), with $\alpha > 0$ is defined by the mass constraint (1.8).

Proof. Stationary solutions to (1.2) - (1.4) satisfy

$$\begin{cases} 0 = \partial_{xx}c(x) + \partial_x((x + \eta\delta\mu)c(x)), & x \in (-1, 1), \\ 0 = c(-1) - \mu_-, \\ 0 = c(1) - \mu_+, \end{cases}$$

together with the flux condition at the boundary:

$$\begin{cases} \partial_x c(-1) + (-1 + \eta\delta\mu)c(-1) = 0, \\ \partial_x c(1) + (1 + \eta\delta\mu)c(1) = 0. \end{cases}$$

Hence, stationary solutions (c, μ_-, μ_+) of (1.2) - (1.4) are characterized by:

$$\begin{cases} c(x) = c(-1)e^{-\frac{x^2-1}{2} - \alpha\eta(x+1)}, & x \in (-1, 1), \\ \alpha = c(-1)(1 - e^{-2\alpha\eta}), \\ \int_{-1}^1 c(x) dx + c(-1) + c(1) = 1, \\ (\mu_-, \mu_+) = (c(-1), c(1)), \end{cases}$$

where

$$\alpha = c(-1) - c(1) = \delta\mu = \mu_- - \mu_+.$$

Consequently the potential stationary solutions are of the form \tilde{G} or \tilde{G}_α . It remains to verify whether the functions \tilde{G} and \tilde{G}_α satisfy the mass constraint.

For all $\eta > 0$ the function \tilde{G} satisfies the mass constraint. It remains to study the case where $\alpha \neq 0$.

Recalling the definition (1.8) of M_λ , we see that $M_\lambda = M_{-\lambda}$, for all $\lambda > 0$, therefore we need to characterize the set $I = \{M_\lambda, \lambda > 0\}$. We see that

$$\begin{aligned} M_\lambda &= \frac{\lambda e^{\lambda\eta}}{2\sinh(\lambda\eta)} \left(\int_{-1}^1 e^{-\frac{x^2-1}{2} - \lambda\eta(x+1)} dx + e^{-2\lambda\eta} + 1 \right) \\ &= \frac{\lambda}{\sinh(\lambda\eta)} \left(\frac{1}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} \cosh(\lambda\eta x) dx + \cosh(\lambda\eta) \right), \end{aligned}$$

it follows that $\lambda > 0$ is a solution of $M_\lambda = 1$ iff

$$R(\lambda) = 0, \tag{4.23}$$

where R is defined by

$$R(\lambda) = \lambda \left(\frac{1}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} \cosh(\lambda\eta x) dx + \cosh(\lambda\eta) \right) - \sinh(\lambda\eta). \tag{4.24}$$

For $\lambda \geq 1$, from the definition of R , we observe that

$$R(\lambda) \geq \cosh(\lambda\eta) - \sinh(\lambda\eta) > 0.$$

The result then follows from the following technical result.

Lemma 9. *The function R satisfies*

$$R(0) = 0, \quad R(1) > 0, \quad R'(0) = \eta_0 - \eta, \quad R''(\alpha) \geq \eta^2 R(\alpha).$$

Moreover if $\eta > \eta_0$, there exists a unique $\alpha > 0$ defined by (1.8) such that $R(\alpha) = 0$. More precisely its behavior is summarized in the following tables

λ	$] -\infty, 0[$	0	$] 0, +\infty[$
$R(\lambda)$	< 0	0	> 0

Table 1: Case: $\eta < \eta_0$

λ	$] -\infty, -\alpha[$	$-\alpha$	$] -\alpha, 0[$	0	$] 0, \alpha[$	α	$] \alpha, +\infty[$
$R(\lambda)$	< 0	0	> 0	0	< 0	0	> 0

Table 2: Case: $\eta > \eta_0$ where α is defined by (1.8)

Proof. We first notice that R is trivially an odd function. So we only need to study it on \mathbb{R}_+ . We compact notations to $R = \lambda R_1 - \sinh(\eta\lambda)$. An immediate computation leads to

$$R'(\lambda) = \lambda R_1' + R_1 - \eta \cosh(\eta\lambda),$$

and

$$R''(\lambda) = 2R_1'(\lambda) + \lambda R_1''(\lambda) - \eta^2 \sinh(\eta\lambda).$$

The nonnegativity of R_1, R_1'' is an immediate consequence of $\cosh \geq 0$. Detailing the results, we have,

$$\begin{aligned} R''(\lambda) &= 2 \left(\frac{1}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} \eta x \sinh(\lambda\eta x) dx + \eta \sinh(\lambda\eta) \right) \\ &\quad + \lambda \left(\frac{1}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} (\eta x)^2 \cosh(\lambda\eta x) dx + \eta^2 \cosh(\lambda\eta) \right) \\ &\quad - \eta^2 \sinh(\lambda\eta). \end{aligned}$$

Hence, the function R satisfies

$$R(0) = 0, \quad R(1) > 0, \quad R'(0) = \eta_0 - \eta.$$

In particular one has $R'(0) < 0$ iff $\eta > \eta_0$. Moreover performing an integration by parts leads to

$$\left(\frac{1}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} \eta x \sinh(\lambda\eta x) dx + \eta \sinh(\lambda\eta) \right) = \frac{\lambda\eta^2}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} \cosh(\lambda\eta x) dx,$$

and

$$\begin{aligned} R''(\lambda) &= \lambda\eta^2 \int_{-1}^1 e^{-\frac{x^2-1}{2}} \cosh(\lambda\eta x) dx \\ &\quad + \lambda \left(\frac{1}{2} \int_{-1}^1 e^{-\frac{x^2-1}{2}} (\eta x)^2 \cosh(\lambda\eta x) dx + \eta^2 \cosh(\lambda\eta) \right) \\ &\quad - \eta^2 \sinh(\lambda\eta), \\ &= R(\lambda) + \frac{\eta^2\lambda}{2} \int_{-1}^1 (1+x^2) e^{-\frac{x^2-1}{2}} \cosh(\lambda\eta x) dx \end{aligned}$$

from which it follows that

$$\forall \lambda \geq 0, R''(\lambda) \geq \eta^2 R(\lambda).$$

This latter inequality yields that: if $R \geq 0$, then R is a convex function. Consequently, the following alternative holds true

- either $\eta \leq \eta_0$ and $R > 0$ on $]0, \infty[$,
- or $\eta > \eta_0$ and the function R is negative in the neighbourhood of 0^+ . Since $R(1) > 0$, from intermediate value theorem, it follows that there exists $\alpha \in (0, 1)$ such that $R(\alpha) = 0$. Since R is increasing in the neighbourhood of 0^+ , and once it is positive it is convex, R can not decrease after being positive.

Hence this achieves the proof of lemma 9. \square

Recalling equation (4.23) rewrites as $R(\lambda) = 0$, this yields proposition 8. \square

5 The comparison principle and its consequences

We start noticing that there is no direct comparison principle on (1.2) - (1.4). In this section, we first establish a concentration comparison principle on the cumulated distribution functions (1.10), reminiscent of [19], and analogous to the radially symmetric Keller-Segel system, see for instance [4, 18] and references therein.

5.1 Comparison principle for Fokker Planck like equation with attachment detachment dynamics on the boundary

We first notice that (1.2) - (1.4) is a specific case of a more general class of Fokker Planck equation

$$\begin{cases} \partial_t c(t, x) - \partial_{xx} c(t, x) - \partial_x((x + \delta(t))c(t, x)) = 0, & x \in (-1, 1), \\ \partial_x c(t, -1) + (-1 + \delta(t))c(t, -1) = \frac{d}{dt} \mu_-(t), \\ \partial_x c(t, 1) + (1 + \delta(t))c(t, 1) = \frac{d}{dt} \mu_+(t), \\ \frac{d}{dt} \mu_-(t) = c(t, -1) - \mu_-(t), \\ \frac{d}{dt} \mu_+(t) = c(t, 1) - \mu_+(t). \end{cases} \quad (5.25)$$

Recalling the definition (1.10) of the cumulated distribution C , we see that the integrated (in space) version of (5.25) is

$$\begin{cases} \partial_t C(t, x) - \partial_{xx} C(t, x) - (x + \delta(t)) \partial_x C(t, x) = 0, & x \in (-1, 1), \\ C(t, -1) = \mu_-(t), & C(t, 1) = 1 - \mu_+(t), \\ \frac{d}{dt} \mu_-(t) = \partial_x C(t, -1) - \mu_-(t), \\ \frac{d}{dt} \mu_+(t) = \partial_x C(t, 1) - \mu_+(t). \end{cases} \quad (5.26)$$

And we have a natural concept of supersolution and subsolution.

Definition 10. A supersolution (resp. subsolution) to (5.26) is a nondecreasing function \bar{C} (resp. \underline{C}) satisfying

$$\begin{cases} \partial_t \bar{C}(t, x) - \partial_{xx} \bar{C}(t, x) - (x + \delta(t)) \partial_x \bar{C}(t, x) \geq 0, & x \in (-1, 1), \\ \bar{C}(t, -1) = \bar{\mu}_-(t), & \bar{C}(t, 1) = 1 - \bar{\mu}_+(t), \\ \frac{d}{dt} \bar{\mu}_-(t) \geq \partial_x \bar{C}(t, -1) - \bar{\mu}_-(t), \\ \frac{d}{dt} \bar{\mu}_+(t) \leq \partial_x \bar{C}(t, 1) - \bar{\mu}_+(t). \end{cases} \quad (5.27)$$

with similar definition for a subsolution by changing \geq into \leq .

We now state the concentration comparison principle for the Fokker Planck like equation with attachment detachment dynamics on the boundary.

Lemma 11. *Let \bar{C}, \underline{C} be respectively smooth super and subsolution to (5.26) associated to the functions $\bar{\delta}, \underline{\delta}$ and defined on $[0, T] \times [-1, 1]$. Assume that*

$$\forall x \in [-1, 1] \quad \bar{C}(0, x) \geq \underline{C}(0, x), \quad (5.28)$$

and

$$\forall t \geq 0 \quad \bar{\delta}(t) \geq \underline{\delta}(t). \quad (5.29)$$

Then, the following inequality holds

$$\forall t \in (0, T), \forall x \in [-1, 1] \quad \bar{C}(t, x) \geq \underline{C}(t, x). \quad (5.30)$$

Remark 12. *From inequality (5.28) taken in $x = -1$ and $x = 1$ it follows that $\bar{\mu}_-(0) \geq \underline{\mu}_-(0)$ and $\bar{\mu}_+(0) \leq \underline{\mu}_+(0)$.*

Remark 13. *From inequality (5.30) taken in $x = -1$ and $x = 1$ it follows that $\bar{\mu}_-(t) \geq \underline{\mu}_-(t)$ and $\bar{\mu}_+(t) \leq \underline{\mu}_+(t)$.*

Proof. Let $Z = \bar{C} - \underline{C}$, $Z_l = \bar{\mu}_- - \underline{\mu}_-$ and $Z_r = \underline{\mu}_+ - \bar{\mu}_+$. We have

$$\begin{cases} \partial_t Z(t, x) - \partial_{xx} Z(t, x) - (x + \bar{\delta}(t)) \partial_x Z(t, x) = (\bar{\delta}(t) - \underline{\delta}(t)) \partial_x \underline{C}(t, x), \\ Z(t, -1) = Z_l(t), \quad Z(t, 1) = Z_r(t), \\ \frac{d}{dt} Z_l(t) \geq \partial_x Z(t, -1) - Z_l(t), \\ \frac{d}{dt} Z_r(t) \leq \partial_x Z(t, 1) - Z_r(t), \\ Z(0, x) \geq 0, \quad x \in (-1, 1), \end{cases} \quad (5.31)$$

and by assumptions (5.28) and (5.29), we know that $(\bar{\delta}(t) - \underline{\delta}(t)) \partial_x \underline{C}(t, x) \geq 0$ for all $x \in (-1, 1)$.

Consider $\varepsilon > 0$. By assumption, see remark 12, $Z_l(0) \geq 0$ and $Z_r(0) \geq 0$. Hence, by continuity in time there exists a time $t_\varepsilon > 0$ such that $Z_l(t) > -\varepsilon$ and $Z_r(t) > -\varepsilon$ on $[0, t_\varepsilon]$. We choose

$$t_\varepsilon = \inf\{t > 0, Z_r(t) = -\varepsilon \text{ or } Z_l(t) = -\varepsilon\}.$$

From the equation, we have immediately $Z(t, x) > -\varepsilon$ on $[0, t_\varepsilon] \times [-1, 1]$. If we assume $t_\varepsilon < +\infty$ then we can assume without loss of generality that we have $Z(t_\varepsilon, -1) = -\varepsilon$. Since we have $Z \geq -\varepsilon$, we have necessarily $\partial_x Z(t_\varepsilon, -1) \geq 0$ and therefore $\frac{d}{dt} Z_l(t_\varepsilon) \geq -(-\varepsilon) = +\varepsilon > 0$. It means that we have

$$Z_l(t) > -\varepsilon, \quad t < t_\varepsilon, \quad \text{and} \quad \frac{d}{dt} Z_l(t_\varepsilon) > 0.$$

Leading by contradiction (we treat the other boundary the same way) to $t_\varepsilon = +\infty$. Letting $\varepsilon \rightarrow 0$, we have the conclusion. \square

5.2 The concentration comparison principle on (1.2) - (1.4)

From now on we denote $\delta\mu = \mu_- - \mu_+$.

We first recall the integrated version of (1.2) - (1.4).

$$\begin{cases} \partial_t C(t, x) - \partial_{xx} C(t, x) - (x + \eta \delta\mu(t)) \partial_x C(t, x) = 0, \quad x \in (-1, 1), \\ C(t, -1) = \mu_-(t), \quad C(t, 1) = 1 - \mu_+(t), \\ \frac{d}{dt} \mu_-(t) = \partial_x C(t, -1) - \mu_-(t), \\ \frac{d}{dt} \mu_+(t) = \partial_x C(t, 1) - \mu_+(t). \end{cases} \quad (5.32)$$

Definition 14. A supersolution (resp. subsolution) to (5.32) is a nondecreasing function \bar{C} (resp. \underline{C}) satisfying

$$\begin{cases} \partial_t \bar{C}(t, x) - \partial_{xx} \bar{C}(t, x) - (x + \eta \delta \bar{\mu}(t)) \partial_x \bar{C}(t, x) \geq 0, & x \in (-1, 1), \\ \bar{C}(t, -1) = \bar{\mu}_-(t), & \bar{C}(t, 1) = 1 - \bar{\mu}_+(t), \\ \frac{d}{dt} \bar{\mu}_-(t) \geq \partial_x \bar{C}(t, -1) - \bar{\mu}_-(t), \\ \partial_x \bar{C}(t, 1) - \bar{\mu}_+(t) \geq \frac{d}{dt} \bar{\mu}_+(t), \end{cases} \quad (5.33)$$

with similar definition for a subsolution by changing \geq into \leq .

We now state the concentration comparison principle for the nonlinear model.

Lemma 15 (Comparison principle). *Let \bar{C} and \underline{C} be respectively smooth super and subsolution to (5.32) defined on $[0, T] \times [-1, 1]$. Assume that*

$$(\forall x \in [-1, 1]) \bar{C}(0, x) \geq \underline{C}(0, x) \text{ and } \bar{\mu}_-(0) + \underline{\mu}_+(0) > \underline{\mu}_-(0) + \bar{\mu}_+(0). \quad (5.34)$$

Then, the following inequality holds

$$(\forall t \in (0, T)) (\forall x \in [-1, 1]) \quad \bar{C}(t, x) \geq \underline{C}(t, x). \quad (5.35)$$

Remark 16. From the first inequality in (5.34) taken in $x = -1$ and $x = 1$ it follows that $\bar{\mu}_-(0) \geq \underline{\mu}_-(0)$ and $\bar{\mu}_+(0) \leq \underline{\mu}_+(0)$. Hence, the second inequality in (5.34) means that one assumes either $\bar{\mu}_-(0) > \underline{\mu}_-(0)$ or $\bar{\mu}_+(0) < \underline{\mu}_+(0)$.

Remark 17. From inequality (5.35) taken in $x = -1$ and $x = 1$ it follows that $\bar{\mu}_-(t) \geq \underline{\mu}_-(t)$ and $\bar{\mu}_+(t) \leq \underline{\mu}_+(t)$.

Proof. By a simple continuity argument, we have

$$\bar{\mu}_- - \bar{\mu}_+ \geq \underline{\mu}_- - \underline{\mu}_+,$$

on a short time interval $[0, t_0]$ with $t_0 > 0$. Therefore, $Z = \bar{C} - \underline{C}$ satisfies the conditions of lemma 11, hence we can claim that on this interval $\bar{C} \geq \underline{C}$. To extend this inequality for all times, we need a bootstrap argument. Because of the initial strict inequality we can claim that $\bar{C}(0, x) \not\equiv \underline{C}(0, x)$. Then by a standard maximum principle argument, we have that $\bar{C}(t, x) - \underline{C}(t, x) > 0$ on $]0, t_0[\times]-1, 1[$. The bootstrap argument is based on Hopf lemma. So, if $\bar{\mu}_- = \underline{\mu}_-$ at time t_0 , then we have $\partial_x(\bar{C}(t, -1) - \underline{C}(t, -1)) > 0$ and thereby $\frac{d}{dt}(\bar{\mu}_- - \underline{\mu}_-)(t_0) > 0$, which leads to a contradiction. The other side of the boundary is treated the same way. \square

5.3 Comparison to remarkable subsolutions

A practical example of subsolution (supersolution) is the following. Consider the real numbers $(\mu_-^\lambda, \mu_+^\lambda)$ and the functions G^λ and C_λ defined by

$$\begin{cases} (G^\lambda(x), \mu_-^\lambda, \mu_+^\lambda) = \frac{1}{e^{\eta\lambda} + e^{-\eta\lambda} + \int_{-1}^1 e^{-\eta\lambda x + \frac{1-x^2}{2}} dx} \left(\int_{-1}^x e^{-\eta\lambda y + \frac{1-y^2}{2}} dy, e^{\eta\lambda}, e^{-\eta\lambda} \right), \\ C_\lambda(x) = \mu_-^\lambda + \int_{-1}^x G^\lambda(y) dy. \end{cases} \quad (5.36)$$

λ	$] -\infty, 0[$	0	$] 0, +\infty[$
C_λ	subsolution	solution	supersolution

Table 3: Case: $\eta < \eta_0$.

λ	$] -\infty, -\alpha[$	$-\alpha$	$] -\alpha, 0[$	0	$] 0, \alpha[$	α	$] \alpha, +\infty[$
C_λ	subsolution	solution	supersolution	solution	subsolution	solution	supersolution

Table 4: Case: $\eta > \eta_0$.

Lemma 18. *Let α and η_0 be respectively defined by (1.8) and (1.9). The function C_λ , defined by (5.36), is either a solution, or a subsolution, or a supersolution to (5.32) according to the following tables*

Proof. Denote $\delta\mu^\lambda = \mu_-^\lambda - \mu_+^\lambda$, by construction we have

$$\begin{cases} \partial_t C_\lambda(x) - \partial_{xx} C_\lambda(x) - (x + \eta\delta\mu^\lambda)\partial_x C_\lambda(x) = \eta(\lambda - \delta\mu^\lambda)\partial_x C_\lambda(x), \\ C_\lambda(-1) = \mu_-^\lambda, \\ C_\lambda(1) = \mu_+^\lambda, \\ \frac{d}{dt}\mu_-^\lambda = 0 = \partial_x C_\lambda(-1) - \mu_-^\lambda, \\ \frac{d}{dt}\mu_+^\lambda = 0 = \partial_x C_\lambda(1) - \mu_+^\lambda. \end{cases} \quad (5.37)$$

So that, since $\partial_x C_\lambda \geq 0$, depending on the sign of $\lambda - \delta\mu^\lambda$, C_λ is a super or a subsolution to (5.32). Recalling the definition (4.24) of the function R , we notice that

$$\lambda - \delta\mu^\lambda = 2 \frac{R(\lambda)}{e^{\eta\lambda} + e^{-\eta\lambda} + \int_{-1}^1 e^{-\eta\lambda x + \frac{1-x^2}{2}} dx}. \quad (5.38)$$

Referring to Table 1 and Table 2, we end up with the Table 3 and Table 4. □

6 Asymptotic control of the boundary terms

We recall that the model is globally well posed and that we always have $\mu_- \leq 1$ and $\mu_+ \leq 1$ by construction. We introduce the following functions

$$\bar{\delta}(t) = \sup_{t' > t} \delta\mu(t'), \quad \underline{\delta}(t) = \inf_{t' > t} \delta\mu(t'). \quad (6.39)$$

By definition we have

$$\lim_{t \rightarrow +\infty} \bar{\delta}(t) = \limsup_{t \rightarrow +\infty} \delta\mu(t), \quad \lim_{t \rightarrow +\infty} \underline{\delta}(t) = \liminf_{t \rightarrow +\infty} \delta\mu(t).$$

We now consider the general drift diffusion equation (5.25) with δ replaced by $\bar{\delta}$ or $\underline{\delta}$. Applying Lemma 11, with $\bar{\mu}_\pm, \bar{c}$ (resp. $\underline{\mu}_\pm, \underline{c}$) solutions to (5.25) with $\delta = \bar{\delta}$ (resp. $\delta = \underline{\delta}$), we know that the following inequality holds for all $t > 0$ and $x \in [-1, 1]$

$$\underline{\mu}_-(t) + \int_{-1}^x \underline{c}(t, y) dy \leq \mu_-(t) + \int_{-1}^x c(t, y) dy \leq \bar{\mu}_-(t) + \int_{-1}^x \bar{c}(t, y) dy.$$

In particular, we have

$$\forall t > 0, \quad \delta \underline{\mu}(t) \leq \delta \mu(t) \leq \delta \bar{\mu}(t).$$

We then use the following convenient result that we prove for sake of completeness.

Proposition 19. *Assume that $\int_{-1}^1 c^0(x) \log c^0(x) dx < +\infty$ and that the function δ converges towards a finite limit δ_0 . Then the solution (c, μ_-, μ_+) to (5.25) with initial condition (c^0, μ_-^0, μ_+^0) converges to the unique steady state of the equation with constant δ_0 defined by*

$$(\bar{c}, \bar{\mu}_-, \bar{\mu}_+) = \frac{1}{\int_{-1}^1 e^{-\frac{x^2-1}{2}-\eta\delta_0 x} dx + e^{\eta\delta_0} + e^{-\eta\delta_0}} \left(e^{-\frac{x^2-1}{2}-\eta\delta_0 x}, e^{\eta\delta_0}, e^{-\eta\delta_0} \right).$$

Proof. By assumption on the initial data, the relative entropy

$$\mathcal{H}(t) = \int_{-1}^1 c(t, x) \log \frac{c(t, x)}{\bar{c}(x)} dx + \mu_-(t) \log \frac{\mu_-(t)}{\bar{\mu}_-(t)} + \mu_+(t) \log \frac{\mu_+(t)}{\bar{\mu}_+(t)}$$

is finite at $t=0$. The function $\mathcal{H}(t)$ is nonnegative and vanishes only in case of equality $(c, \mu_-, \mu_+) = (\bar{c}, \bar{\mu}_-, \bar{\mu}_+)$ since

$$\mathcal{H}(t) = \int_{-1}^1 \bar{c}(x) h \left(\frac{c(t, x)}{\bar{c}(x)} \right) dx + \bar{\mu}_+ h \left(\frac{\mu_+(t)}{\bar{\mu}_+} \right) + \bar{\mu}_- h \left(\frac{\mu_-(t)}{\bar{\mu}_-} \right),$$

with $h(x) = x \log x - x + 1 \geq 0$ being a convex function such that $h(1) = 0$.

Differentiating \mathcal{H} , we obtain

$$\begin{aligned} \frac{d}{dt} \mathcal{H}(t) &= -\frac{d}{dt} \mu_-(t) \log \frac{c(t, -1)}{\mu_-(t)} - \frac{d}{dt} \mu_+(t) \log \frac{c(t, 1)}{\mu_+(t)} \\ &\quad - \int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta(t)) (\partial_x \log c(t, x) + x + \eta \delta_0) dx. \end{aligned}$$

Moreover we see that

$$\begin{aligned} &\int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta(t)) (\partial_x \log c(t, x) + x + \eta \delta_0) dx \\ &= - \int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta_0)^2 dx \\ &\quad + \eta (\delta(t) - \delta_0) \int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta_0) dx, \end{aligned}$$

and

$$\begin{aligned} &\eta (\delta(t) - \delta_0) \int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta_0) dx \\ &\leq \eta |\delta(t) - \delta_0| \left(\int_{-1}^1 c(t, x) dx \right)^{1/2} \left(\int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta_0)^2 dx \right)^{1/2} \\ &\leq \frac{1}{2} \eta^2 |\delta(t) - \delta_0|^2 + \frac{1}{2} \left(\int_{-1}^1 c(t, x) dx \right) \left(\int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta_0)^2 dx \right) \\ &\leq \frac{1}{2} \eta^2 |\delta(t) - \delta_0|^2 + \frac{1}{2} \int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta_0)^2 dx. \end{aligned}$$

Consequently we obtain

$$\begin{aligned} \frac{d}{dt} \mathcal{H}(t) &\leq -(c(t, -1) - \mu_-(t)) \log \frac{c(t, -1)}{\mu_-(t)} - (c(t, 1) - \mu_+(t)) \log \frac{c(t, 1)}{\mu_+(t)} \\ &\quad - \frac{1}{2} \int_{-1}^1 c(t, x) (\partial_x \log c(t, x) + x + \eta \delta_0)^2 dx + \frac{1}{2} \eta^2 |\delta(t) - \delta_0|^2. \end{aligned}$$

Define the functions \mathcal{D}_\pm and \mathcal{D} by

$$\begin{aligned} \mathcal{D}_\pm(t) &= (c(t, \pm 1) - \mu_\pm(t)) \log \frac{c(t, \pm 1)}{\mu_\pm(t)} \geq 0, \\ \mathcal{D}(t) &= \mathcal{D}_-(t) + \mathcal{D}_+(t) + \frac{1}{2} \mathcal{I}(c|\bar{c}). \end{aligned}$$

Let K denote any constant depending only on the values of $\bar{\mu}_\pm, \bar{c}$. We have

$$\begin{aligned} \left\| \partial_x \left(\frac{c(t, \cdot)}{\bar{c}} \right) \right\|_1 &\leq \left\| \frac{1}{\bar{c}} \right\|_\infty \left\| \sqrt{c(t, \cdot)} \right\|_2 \left\| \sqrt{c(t, \cdot)} \partial_x \log \frac{c(t, \cdot)}{\bar{c}} \right\|_2 \\ &\leq K \sqrt{\mathcal{I}(c|\bar{c})} \leq K \sqrt{\mathcal{D}(t)}. \end{aligned}$$

Denoting

$$M(t) = \sup_{x \in [-1, 1]} \frac{c(t, x)}{\bar{c}(x)}, \quad m(t) = \inf_{x \in [-1, 1]} \frac{c(t, x)}{\bar{c}(x)},$$

we obtain

$$\left\| \frac{c(t, \cdot)}{\bar{c}} - m \right\|_\infty + \left\| \frac{c(t, \cdot)}{\bar{c}} - M \right\|_\infty + |M - m| \leq K \sqrt{\mathcal{D}(t)}.$$

From this, we infer

$$m(t) \int_{-1}^1 \bar{c}(x) dx \leq \int_{-1}^1 c(t, x) dx \leq (m(t) + K \sqrt{\mathcal{D}(t)}) \int_{-1}^1 \bar{c}(x) dx,$$

which translates into

$$m(t)(1 - \bar{\mu}_+ - \bar{\mu}_-) \leq 1 - \mu_+(t) - \mu_-(t) \leq (m(t) + K \sqrt{\mathcal{D}(t)})(1 - \bar{\mu}_+ - \bar{\mu}_-),$$

hence

$$m \leq 1/(1 - \bar{\mu}_- - \bar{\mu}_+) \leq K.$$

Moreover, adding $m(t)(\bar{\mu}_+ + \bar{\mu}_-) - 1$ we get

$$m(t) - 1 \leq m(t)(\bar{\mu}_+ + \bar{\mu}_-) - \mu_+(t) - \mu_-(t) \leq m(t) - 1 + K \sqrt{\mathcal{D}(t)}(1 - \bar{\mu}_+ - \bar{\mu}_-),$$

ending up with

$$|m(t) - 1| \leq |m(t)(\bar{\mu}_+ + \bar{\mu}_-) - \mu_+(t) - \mu_-(t)| + K \sqrt{\mathcal{D}(t)}(1 - \bar{\mu}_+ - \bar{\mu}_-).$$

Finally, we notice that

$$(c(t, 1) - \mu_+(t)) \log \frac{c(t, 1)}{\mu_+(t)} \geq \frac{(c(t, 1) - \mu_+(t))^2}{c(t, 1) + \mu_+(t)} \geq \bar{\mu}_+ \frac{(\frac{c(t, 1)}{\bar{\mu}_+} - \frac{\mu_+(t)}{\bar{\mu}_+})^2}{\frac{c(t, 1)}{\bar{\mu}_+} + \frac{\mu_+(t)}{\bar{\mu}_+}}$$

$$\geq \frac{\bar{\mu}_+(c(t,1) - \mu_+(t))^2}{K(1 + \sqrt{\mathcal{D}(t)})}.$$

This can be summarized as

$$\begin{aligned} |c(t,1) - \mu_+(t)| + |c(t,-1) - \mu_-(t)| &\leq K(\sqrt{D_+(t)} + \sqrt{D_-(t)})\sqrt{1 + \sqrt{\mathcal{D}(t)}} \\ &\leq K\sqrt{D(t) + D(t)^{3/2}}. \end{aligned}$$

Putting everything together, we have

$$|\mu_+(t) - m\bar{\mu}_+| \leq |\mu_+(t) - c(t,1)| + |c(t,1) - \mu_+(t)| \leq K\sqrt{D(t) + \mathcal{D}(t)^{3/2}},$$

and finally $|m(t) - 1| \leq K\sqrt{D(t) + \mathcal{D}(t)^{3/2}}$. This leads finally to

$$|\mu_+(t) - \bar{\mu}_+| + |\mu_-(t) - \bar{\mu}_-| + \|c(t, \cdot) - \bar{c}\|_\infty \leq K\sqrt{D(t) + \mathcal{D}(t)^{3/2}}.$$

By construction, since $\mathcal{H} \geq 0$, $\limsup -\mathcal{D} + \eta|\delta - \delta_0|^2 \geq 0$. Since the last part goes to 0, this leads to $\liminf \mathcal{D}(t) = 0$ and thereby to $\liminf \mathcal{H}(t) = 0$. Finally, let $\varepsilon > 0$. Assume $\limsup \mathcal{H} \geq \varepsilon$. There exists $C(\varepsilon) > 0$ such that $\mathcal{H}(t) \geq C(\varepsilon)$ for all t . \square

Let

$$G(\delta) = \frac{e^{\eta\delta} - e^{-\eta\delta}}{\int_{-1}^1 e^{-\frac{x^2-1}{2} - \eta\delta x} dx + e^{\eta\delta} + e^{-\eta\delta}} = \frac{2\delta \sinh(\eta\delta)}{F(\delta)},$$

where we have kept the notation (3.21) for F .

Applying proposition 19 with $\delta = \underline{\delta}, \bar{\delta}$, it yields the following result.

Lemma 20. *The solutions $(\bar{c}, \bar{\mu}_-, \bar{\mu}_+)$ and $(\underline{c}, \underline{\mu}_-, \underline{\mu}_+)$ to (5.25) for respectively $\bar{\delta}$ and $\underline{\delta}$ defined by (6.39) satisfy*

$$\begin{aligned} \lim_{t \rightarrow \infty} \delta \underline{\mu}(t) &= G(\lim_{t \rightarrow \infty} \underline{\delta}(t)), \\ \lim_{t \rightarrow \infty} \delta \bar{\mu}(t) &= G(\lim_{t \rightarrow \infty} \bar{\delta}(t)). \end{aligned}$$

Lemma 21. *Let (c, μ_-, μ_+) be solution to (1.2) - (1.4). Let $\bar{\delta}_\infty = \limsup_{t \rightarrow \infty} \delta \mu(t)$ and $\underline{\delta}_\infty = \liminf_{t \rightarrow \infty} \delta \mu(t)$, then the following inequalities hold*

$$G(\underline{\delta}_\infty) \leq \underline{\delta}_\infty \leq \bar{\delta}_\infty \leq G(\bar{\delta}_\infty).$$

Proof. By definition (6.39) of the functions $\underline{\delta}$ and $\bar{\delta}$, we see that $\lim_{t \rightarrow \infty} \underline{\delta}(t) = \liminf_{t \rightarrow \infty} \delta \mu(t)$ and $\lim_{t \rightarrow \infty} \bar{\delta}(t) = \limsup_{t \rightarrow \infty} \delta \mu(t)$.

Using lemma 11, it follows that for all time

$$\delta \underline{\mu}(t) \leq \delta \mu(t) \leq \delta \bar{\mu}(t),$$

hence the result follows from lemma 20. \square

As a consequence, we have

Lemma 22. *Let (c, μ_-, μ_+) be solution to (1.2) - (1.4). Then we have*

$$-\alpha \leq \underline{\delta}_\infty \leq \bar{\delta}_\infty \leq +\alpha.$$

Furthermore, if we can ensure $\underline{\delta}_\infty > 0$ (resp. $\bar{\delta}_\infty < 0$), then we have $\lim_{+\infty} \delta \mu = \alpha$ (resp. $-\alpha$).

Proof. We first recall that the steady states of the system (1.2) - (1.4) are characterized by $\delta\mu = \delta \in \{-\alpha, 0, \alpha\}$ where $0 \leq \alpha \leq 1$ and with $\alpha = 0$ if $\eta \leq \eta_0$ and α is the positive solution in $]0, 1[$ of equation (1.8) if $\eta > \eta_0$.

We prove it only for one side (the other comes from a symmetry argument). If $\bar{\delta}_\infty \leq 0$, then the proof is achieved. If $\bar{\delta}_\infty > 0$, then the inequality $\bar{\delta}_\infty \leq G(\bar{\delta}_\infty)$ is equivalent to $R(\bar{\delta}_\infty) \leq 0$ (notations from the proof of lemma 8) and thereby to $\bar{\delta}_\infty \leq \alpha$. \square

As a final consequence, we have a few nonquantitative convergence

Proof. From lemmas 20, lemma 21 and lemma 22 we infer that if we have a limit for $\delta\mu$ and we are in position to apply lemma 19. The last point is a consequence of lemma 18. \square

7 Conclusion

Recently the first world cell race was organized by Maiuri et al [20]. During this race, different types of cells were put on one-dimensional adhesive tracks. Collecting cell trajectories showed a correlation between instantaneous cell velocity and persistence time, defined as the average time a cell maintains its direction of movement.

Later in [21], the authors proposed a 1D model of cell crawling migration which describes the dynamics of a marker of back-polarity (of concentration $c(x, t)$), binding to actin filaments subjected to a retrograde flow of constant value in the cell $V(t)$. The basic idea of this coupling model is that $V(t)$ is itself driven by a front-back asymmetry in $c(x, t)$. Assuming a fast dynamics of the marker (relative to the actin flow), the average concentration is approximated by the quasi-stationary state:

$$\bar{c}(x) = Ce^{-Vx/D},$$

where D is the diffusion coefficient of c . The dynamics of the actin flow velocity V is given by

$$\frac{dV}{dt} = \gamma(V - V^*),$$

with

$$V^* = \beta \left(\frac{c(0, t)}{C_s + c(0, t)} - \frac{c(L, t)}{C_s + c(L, t)} \right),$$

where γ^{-1} is a relaxation time scale associated with actin flow fluctuations, β is a parameter controlling the intensity of the coupling (also corresponding to the maximal actin speed), C_s is a saturation parameter for the marker concentration (meaning the maximal concentration of "activated" molecules). Adding some stochasticity to the previous model (with noise in both c and V) the author of [21] predicts a rich motility phase diagram in the parameters β and C_s . The phases are: (i) "diffusive" cell migration, when β is low, (ii) "persistent" migration, when β is large, and (iii) "intermittent" migration (corresponding to the low C_s regime), when the cell stochastically switches between "diffusive" and "persistent" motility. It was also shown in [21] that experimental cell trajectories could be broadly classified into these three phases.

The present paper considers the full dynamics of a 1D model which is based on the same ideas as those set in [21]. Here we prove that it yields the same state phase behavior, hence giving a mathematical justification to the assumptions made in [21]. Future work [14] would be to extend the results of this paper to a two-dimensional geometry with free boundary.

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References

- [1] E. BARNHART, K.-C. LEE, G. M. ALLEN, J. A. THERIOT, AND A. MOGILNER, *Balance between cell-substrate adhesion and myosin contraction determines the frequency of motility initiation in fish keratocytes*, Proc Natl Acad Sci U S A, 112(16):5045-5050, Apr 2015.
- [2] L. BERLYAND, J. FUHRMANN AND V. RYBALKO. *Bifurcation of traveling waves in a Keller-Segel type free boundary model of cell motility*. Commun. Math. Sci. 16, No. 3, 735-762 (2018). 1
- [3] L. BERLYAND AND V. RYBALKO. *Stability of steady states and bifurcation to traveling waves in a free boundary model of cell motility*, (2019). 1
- [4] P. BILER, G. KARCH, P. LAURENÇOT, AND T. NADZIEJA. *The problem for radially symmetric solutions of a chemotaxis model in the plane*. Mathematical Methods in the Applied Sciences, 29(13):1563-1583 (2006). 5
- [5] C. BLANCH-MERCADER, J., CASADEMUNT, *Spontaneous motility of actin lamellar fragments*, Phys. Rev. Lett., 110, (2013). 2
- [6] A. BLANCHET, *On the parabolic-elliptic patlak-keller-segel system in dimension 2 and higher*, Séminaire Laurent Schwarz - EDP et applications, (2011-2012). 1
- [7] M. J. CÁCERES AND R. SCHNEIDER, *Blow-up, steady states and long time behaviour of excitatory-inhibitory nonlinear neuron models*, Kinetic and Related Models, 10(3), (2017). 1
- [8] A. CALLAN-JONES, J.-F. JOANNY AND J. PROST, *Viscous-Fingering-Like Instability of Cell Fragments*, Phys. Rev. Lett., 100(25), (2008) 2
- [9] A. CALLAN-JONES AND R. VOITURIEZ, *Active gel model of amoeboid cell motility*, New Journal of Physics, 15 (2013). 2
- [10] V. CALVEZ, N. MEUNIER AND R. VOITURIEZ, *A one-dimensional Keller-Segel equation with a drift issued from the boundary* Boundary, C. R. Math. Acad. Sci. Paris, 348, 629-634, (2010).
- [11] V. CALVEZ, R. HAWKINS, N. MEUNIER AND R. VOITURIEZ, *Analysis of a non local model for spontaneous cell polarisation*, SIAM J. Appl. Math., 72 (2), 594-622, (2012). 1
- [12] J. A. CARRILLO, M. D M GONZÁLEZ, M. P. GUALDANI, AND M. E. SCHONBEK, *Classical solutions for a nonlinear fokker-planck equation arising in computational neuroscience*. Communications in Partial Differential Equations, 38(3):385-409, (2013). 1
- [13] C. ETCHEGARAY, N. MEUNIER AND R. VOITURIEZ, *Analysis of a non local and non linear Fokker-Planck model for cell crawling migration*, SIAM J. Appl. Math., 72 (2), 594-622, (2017). 1, 1

- [14] C. ETCHEGARAY, N. MEUNIER AND R. VOITURIEZ, *A 2D multiscale model for unicellular crawling: universality of migration and trajectories*, submitted. [1](#), [7](#)
- [15] L. C. EVANS, *Partial differential equations*, vol. 19 of Graduate Studies in Mathematics, American Mathematical Society, Providence, RI, (1998).
- [16] H. GAJEWSKI, *On the uniqueness of solutions to the drift-diffusion model of semiconductor devices*, Mathematical Models and Methods in Applied Sciences, 4(01):121?133, (1994). [3.1](#)
- [17] F. JÜLICHER, K. KRUSE, J. PROST, J.F. JOANNY, *Active behavior of the cytoskeleton*. Phys. Rep.-Rev. Sect. Phys. Lett. 449, 3?28, (2007). [2](#)
- [18] I. KIM AND Y. YAO. *The patlak Keller-Segel model and its variations: Properties of solutions via maximum principle*. SIAM Journal on Mathematical Analysis, 44(2):568?602, (2012). [5](#)
- [19] T. LEPOUTRE, N. MEUNIER et N. MULLER, *Cell polarisation model: the 1D case*, J. Math. Pures Appl., (2012). [1](#), [5](#)
- [20] P. MAIURI, ET AL., *The first world cell race*. Current Biology, 22, pp. R673?R675 (2012). [7](#)
- [21] P. MAIURI, ET AL., *Actin flows mediate a universal coupling between cell speed and cell persistence*. Cell 161, 374? 386 (2015). [1](#), [2](#), [7](#)
- [22] V. MILISIC and D. OELZ *On a structured model for the load dependent reaction kinetics of transient elastic linkages* SIAM J. Math. Anal. 47, no. 3, 2104–2121 (2015). [2](#)
- [23] N. MULLER, ET AL., *A Predictive Model for Yeast Cell Polarization in Pheromone Gradients*, PLoS Comput Biol, 12(4), (2016).
- [24] P. RECHO, T. PUTELAT, AND L. TRUSKINOVSKY, *Contraction-driven cell motility*, Phys. Rev. Lett., 111(10):108102, (2013). [1](#)
- [25] P. RECHO, T. PUTELAT, AND L. TRUSKINOVSKY, *Mechanics of motility initiation and motility arrest in crawling cells*, Journal of Mechanics and Physics of Solids, 84:469 ? 505, (2015). [1](#)
- [26] P. RECHO, T. PUTELAT, AND L. TRUSKINOVSKY, *Mechanical stress as a regulator of cell motility*, Phys. Rev. E, 97(1), 012410, (2018). [1](#)