

A 2D fluid-based model for individual cell crawling

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Abstract

This paper presents the analysis and numerical simulations of a two-dimensional model of single-cell crawling migration, focusing on intracellular dynamics. The fluid-based model relies on the interaction between the actin cytoskeleton and a generic molecular regulator of its activity. The model is formulated as a Poisson problem with Darcy's law, coupled with a nonlocal advection-diffusion equation for the molecular concentration, where the non-local term involves boundary values. Existence and uniqueness of resting and travelling stationary states are established in certain parameter domains, along with linear stability in the resting case. Numerical simulations illustrate both cell regimes. This demonstrates the model's ability to capture key features of cell migration.

Keywords: Cell migration, Darcy law, Nonlinear advection-diffusion equation

1 Introduction

1.1 Motivations: a general rule of cell migration

Cell migration is a fundamental process involved in many physiological and pathological functions, such as immune response, morphogenesis, and cancer metastasis [1, 2]. It depends on a complex intracellular machinery [3]. Therefore, understanding its key features despite the variety of cellular behaviours is a challenging task. Recently, a

biophysical approach showed that even when different migration modes coexist, cell migration follows a very general principle.

In [4], following the First World Cell Race [5], the authors performed and analysed extensive experimental assays in both geometrical settings and migration modes. They found that cell persistence - the directional correlation of trajectories - is exponentially correlated with cell velocity: faster cells migrate more directionally. This coupling was termed the "Universal Coupling between cell Speed and Persistence" (UCSP). Further experiments suggested that it depends on actin flows, which are shared by all cell types. Actin filaments are components of the cell cytoskeleton, the dynamic network of biopolymers responsible for the cell's integrity and force generation. These filaments are polar: they grow by polymerizing at one end and shrink by depolymerizing at the other end. In migrating cells, polymerizing ends are located near the cell membrane, which resists filament growth. As a result, in the cell's frame of reference, actin filaments drift away from the membrane, forming the so-called actin retrograde flows. Large and rapid actin flows are known to enhance cell polarity. Experiments suggest that this may result from the advection of polarity cues, which are molecules involved in the regulation of the cytoskeleton activity. Such molecules may regulate various phenomena, such as contraction or cytoskeleton activity, depending on the cell type. Figure 1 shows the resulting minimal system involving the actin cytoskeleton and the molecular species.

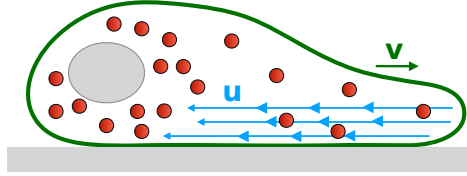


Fig. 1 Illustration of the main ingredients of the physical model introduced in [4]. The cell membrane is depicted in green, the actin filaments in blue, and the molecular species in red. The cell moves forward with velocity $\mathbf{v}$, while the actin filaments drift away from the leading edge with local velocity $\mathbf{u}$ due to actin polymerisation dynamics. Figure reproduced and adapted from [4].

A physical model based on the intracellular feedback loop between actin flows and a generic molecular species was introduced in [4]. The dynamics are described within the cytoplasm, along the one-dimensional cell polarity axis $[0, L]$, $L > 0$. The molecular concentration $c : \mathbb{R}_+ \times [0, L] \rightarrow \mathbb{R}_+$ follows a conservative reaction-advection-diffusion dynamic: molecules diffuse within the cell and are transported by actin flows at a scalar velocity $u : \mathbb{R}_+ \rightarrow \mathbb{R}_+$. Additionally, they are activated at the boundary, acquiring the ability to regulate actin dynamics. The model includes two sources of stochasticity. First, the advection velocity follows a stochastic diffusion process, with its mean value depending on the difference in activated molecular concentration at the two cell ends. The advection-diffusion flux is further perturbed by additive Gaussian white noise in time, which carries spatial correlations.

This work highlighted the powerful idea of a generic mechanism for cell migration, and enabled further analysis of cell trajectories from microscopic features. However,

the model has some limitations. Firstly, the molecular dynamics are one-dimensional and therefore not affected by angular variations of the polarity axis. Secondly, the actin velocity is a global quantity, whose dynamics are defined as a stochastic diffusion process drifting towards its mean value. Its regulation by the molecular species is defined phenomenologically from the boundary molecular concentration. With that in mind, we developed a two-dimensional problem based on a fluid description of the cytoskeleton. This provides a fully spatial description of cell polarisation at both molecular and cytoskeletal scales, resulting in a minimal model of the intracellular physicochemical interactions that lead to cell motion.

1.2 Model under study

In this Subsection, we introduce the mathematical model that is derived and analysed in the course of the article. The justification of the modelling approach will be given in Section 2. Denote $\Omega = B(0, 1)$ the unit disk defining the motionless cell in its frame of reference, and $\mathbf{v} : \mathbb{R}_+ \rightarrow \mathbb{R}^2$ the cell velocity. The actin cytoskeleton is described by a fluid of velocity $\mathbf{u} : \mathbb{R}_+ \times \Omega \rightarrow \mathbb{R}^2$ and pressure $p : \mathbb{R}_+ \times \Omega \rightarrow \mathbb{R}$. We consider a molecular species of cytosolic concentration $c : \mathbb{R}_+ \times \Omega \rightarrow \mathbb{R}_+$, diffusing in the cell body, and carried by the actin flows. The problem for the molecular dynamics writes as follows:

$$\begin{cases} \partial_t c + \operatorname{div}(\mathbf{c}\mathbf{u} - D\nabla c) = 0 & \text{in } \Omega, \\ (D\nabla c - \mathbf{c}\mathbf{u}) \cdot \mathbf{n} = 0 & \text{on } \partial\Omega. \end{cases} \quad (1)$$

In these equations, $D \geq \underline{D}$ is the diffusion coefficient for some $\underline{D} > 0$, and the boundary condition ensures that the molecular mass M is preserved. In the following, it is fixed to $M = 1$. The fluid problem consists in the coupling between a Darcy law and a Poisson-Dirichlet problem. It writes

$$\mathbf{u}(t, \mathbf{x}) + \mathbf{v}(t) = -\nabla p(t, \mathbf{x}) \text{ in } \Omega, \quad (2)$$

$$\begin{cases} -\Delta p = -1 & \text{in } \Omega, \\ p = -\chi k_p(c) & \text{on } \partial\Omega, \end{cases} \quad (3)$$

where $-\chi k_p$ is a Dirichlet boundary term and -1 a sink term quantifying respectively actin polymerisation and depolymerisation. Together, they are responsible for the generation of an inward flow from the boundary, seen in the pressure gradient in Equation (2). The dependence of k_p on the concentration c describes its regulating effect on the actin polymerisation. When k_p is an increasing function of c , the accumulation of activated molecules on a part of the boundary locally decreases the pressure, characterising molecular inhibitors of actin polymerisation. Finally, the cell velocity is obtained from the friction balance between actin flows and passive loads in the cell, and writes

$$\mathbf{v}(t) = \gamma \int_{\partial\Omega} p \mathbf{n} \, d\sigma = -\gamma \chi \int_{\partial\Omega} k_p(c) \mathbf{n} \, d\sigma. \quad (4)$$

In the case of an increasing function k_p , for example for $k_p(c) = c$, the cell velocity rewrites $\mathbf{v}(t) = -\gamma \chi \int_{\partial\Omega} c \mathbf{n} \, d\sigma$ and the molecular species characterises the cell rear.

Hence, from the modelling viewpoint, the necessary assumptions on k_p are its regularity, being increasing, and such that $k_p(0) = 0$. Let us now introduce the following assumptions on k_p :

Hypotheses One has that

- A1.** $k_p \in C^3(\mathbb{R}_+)$ with $\lim_{x \rightarrow +\infty} k_p(x) = 1$,
- A2.** $k_p(0) = 0$ and k_p is monotonically increasing,
- A3.** $\exists A > 0, \forall x \geq 0, xk'_p(x) \leq A$.

A prototype example of a function satisfying Assumptions [A1.-A2.-A3.](#) is

$$k_p(x) = \frac{x}{c_t + x}, \quad (5)$$

for $c_t > 0$. In such a case, [A3.](#) holds with $A = 1/4$.

1.3 Context and plan of the paper

Fluid-based models of cell dynamics are widely used to model a variety of phenomena, see [\[6\]](#) for a review. The physical model developed in [\[4\]](#) follows principles from the active polar gel theory [\[7\]](#). Other works are based on hydrodynamics frameworks.

In [\[8\]](#), linear instability of the interface is established for a model of cell fragment in large friction regime. The model is based on Darcy's law for actin velocity with edge polymerisation and bulk depolymerisation. The actin filaments' orientation is further taken into account in [\[9\]](#). Based on [\[8\]](#), the nonlinear stability of the cell's centre of mass is obtained in [\[10\]](#), and the existence of travelling waves is rigorously established in [\[11\]](#).

Some free boundary models of cell motility focus on the effect of contractility, and investigate stationary states and the emergence of travelling wave solutions [\[12–18\]](#). Following [\[14, 15\]](#), a two-dimensional elliptic problem for the cytoskeleton is coupled with an advection-diffusion for myosin motors in [\[16\]](#). The model presents non-radial stationary states, and bifurcation of travelling waves from radially-symmetric stationary states. Another approach is based on Darcy's law for actin velocity, the Young-Laplace equation for the pressure and an advection-diffusion equation for myosin [\[12, 17\]](#).

Finally, another set of studies follow from [\[19\]](#). The key feature is an active traction force at the boundary driving the dynamics, with a passive cytoskeleton and a diffusive solute regulating the force. This minimal framework can describe either polymerisation or contraction depending on the force sign. Linear and nonlinear analysis show the emergence of unstable state depending on the solute activity, up to bifurcations of multipolar modes. The existence of non-trivial travelling wave solutions is established in [\[20\]](#). Recent work investigates the stabilising effect of the membrane [\[21\]](#). A similar model without molecular species was also studied in [\[22\]](#).

In this work, we focus on the justification of the model from [\[4\]](#) in a two-dimensional spatial setting for a disk-shaped cell. This paper is organised as follows: in [Section 2](#),

we present the model under study. In Section 3, we give some energy estimates, put to light both resting and travelling stationary regimes under given conditions, and provide conditions for the linear stability of the resting stationary state. In Section 4, we perform numerical simulations of the system using the finite volumes method. The simulations illustrate the two regimes and provide phase diagrams depicting transition between both. These results are discussed in Section 5. Finally, Section 6 summarizes our findings.

2 The 2D model and some energy estimates

In this Section, we introduce the modelling approach leading to Problem (1)–(2)–(3)–(4), and provide related mathematical estimates. Subsection 2.1 is devoted to the introduction of the modelling approach, while Subsection 2.2 details the final model derivation. Then, some estimates are given in Subsection 3.1.

2.1 Modelling approach

In this Subsection, we present the model based on the coupling of a molecular species with a fluid description of the cell. The cell is assumed to spread on the surface with constant thickness, reducing to a two-dimensional description. In order to concentrate on intracellular dynamics, the cell deformations are ignored, and the cell is represented by a 2D disc that simultaneously contains passive components (such as the centrosome and nucleus) that are inert for migration but rub against the substrate during displacement, and a viscous fluid that represents the cytoskeleton [23]. These passive components are considered a non-local passive source of friction forces. Let us define $t \mapsto \Omega(t)$ the moving cell domain with global velocity $\mathbf{V} : \mathbb{R}_+ \rightarrow \mathbb{R}^2$. In the following, we derive the constitutive equations for the fluid, including its active properties.

2.1.1 Fluid problem

For $t > 0$ and $\mathbf{X} \in \Omega(t)$, let us denote $\tilde{P}(t, \mathbf{X})$ the fluid pressure and $\tilde{\mathbf{U}}(t, \mathbf{X})$ the actin velocity field. The viscous fluid is characterised by two physical conservation laws: the force balance principle and the continuity equation on the actin density.

Force balance principle

In the setting of low Reynolds number, in the frame of reference of the lab, the force balance principle leads to the Stokes equation given by

$$\begin{aligned} -\eta \Delta \tilde{\mathbf{U}}(t, \mathbf{X}) + \nabla \tilde{P}(t, \mathbf{X}) &= -\xi(\tilde{\mathbf{U}}(t, \mathbf{X}) + \mathbf{V}(t)) && \text{in } \Omega(t), \\ \eta \left(\nabla \tilde{\mathbf{U}}(t, \mathbf{X}) + {}^t \nabla \tilde{\mathbf{U}}(t, \mathbf{X}) \right) \cdot \mathbf{n} - \tilde{P}(t, \mathbf{X}) \mathbf{n} &= K_p \mathbf{n} && \text{on } \partial\Omega(t), \end{aligned}$$

where $\eta \in \mathbb{R}_+$ is the fluid viscosity and $\mathbf{n}$ the outward unit normal to the boundary. The right-hand-side of the first equation corresponds to the force arising from actin rubbing on the substrate, with $\xi \in \mathbb{R}_+$ an effective friction coefficient. The boundary condition is defined using the normal component of the stress tensor and involves the force K_p related to actin polymerisation at the boundary.

Continuity equation

For $\varepsilon > 0$ a small parameter homogeneous to the inverse of a pressure, we introduce the actin density $\tilde{\rho}_\varepsilon(t, \mathbf{X})$, defined for $t > 0$ and $\mathbf{X} \in \Omega(t)$. The continuity equation inside the domain writes

$$\begin{aligned} \frac{\partial}{\partial t} \tilde{\rho}_\varepsilon(t, \mathbf{X}) + \operatorname{div} (\tilde{\rho}_\varepsilon(t, \mathbf{X})(\tilde{\mathbf{U}}(t, \mathbf{X}) + \mathbf{V}(t))) &= -K_d \tilde{\rho}_\varepsilon(t, \mathbf{X}) \quad \text{in } \Omega(t), \\ \tilde{\rho}_\varepsilon(t, \mathbf{X}) &= \rho_0 - \varepsilon K_p \quad \text{on } \partial\Omega(t), \end{aligned}$$

where K_d is a constant depolymerisation rate acting on the whole domain and the actin advection field $\tilde{\mathbf{U}}(t, \mathbf{X}) + \mathbf{V}(t)$ is expressed in the frame of reference of the lab. The Dirichlet boundary condition accounts for polymerisation taking place at the edge of the cell, with $\rho_0 \in \mathbb{R}_+$. Hence, εK_p represents a decrease from the typical actin polymerisation that would yield a null force in the boundary term of the Stokes Problem. Following [23], we make the assumption that the pressure is linear in the difference between the actin density and the resting value ρ_0 :

$$\tilde{P}_\varepsilon = \frac{1}{\varepsilon}(\tilde{\rho}_\varepsilon - \rho_0) \quad \text{in } \Omega(t).$$

This means that the pressure tends to maintain a fluid density close to $\rho_0 > 0$.

2.1.2 Cell velocity

The global cell velocity is obtained from the mechanical equilibrium between the fluid and the internal components generating passive friction forces with cell displacement. Under the assumption that the actin flows generate friction forces in the frame of reference of the lab, one can write

$$\xi_1 \mathbf{V}(t) + \xi \int_{\Omega(t)} \tilde{\mathbf{U}}(t, \mathbf{x}) + \mathbf{V}(t) \, d\mathbf{x} = 0,$$

where $\xi_1 > 0$ is a global cell friction coefficient. Equivalently, one can write

$$\mathbf{V}(t) = -\frac{\xi}{\xi_1 + \xi|\Omega(0)|} \int_{\Omega(t)} \tilde{\mathbf{U}}(t, \mathbf{X}) \, d\mathbf{X}.$$

2.1.3 Formulation in a motionless domain

The fluid problem is now written on the fixed domain $\Omega := \Omega(0) = B(0, R)$, with $R > 0$. As $(\tilde{P}, \tilde{\mathbf{U}}, \tilde{\rho}_\varepsilon)$ are defined on $\Omega(t)$, we denote $(P, \mathbf{U}, \rho_\varepsilon)$ their analogue on Ω . Since the domain velocity is a global quantity, only the advection velocity in the continuity equation is modified by the change of reference domain, and the expression for the cell velocity remains the same in the new reference domain. The fluid problem writes

$$\begin{cases} -\eta \Delta \mathbf{U}(t, \mathbf{x}) + \nabla P(t, \mathbf{x}) = -\xi(\mathbf{U}(t, \mathbf{x}) + \mathbf{V}(t)) & \text{in } \Omega, \\ \eta(\nabla \mathbf{U}(t, \mathbf{x}) + {}^t \nabla \mathbf{U}(t, \mathbf{x})) \cdot \mathbf{n} - P(t, \mathbf{x}) \mathbf{n} = K_p \mathbf{n} & \text{on } \partial\Omega, \end{cases}$$

together with

$$\begin{cases} \frac{\partial}{\partial t} \rho_\varepsilon(t, \mathbf{x}) + \operatorname{div} (\rho_\varepsilon(t, \mathbf{x}) \mathbf{U}(t, \mathbf{x})) = -K_d \rho_\varepsilon(t, \mathbf{x}) & \text{in } \Omega, \\ \rho_\varepsilon(t, \mathbf{x}) = \rho_0 - \varepsilon K_p & \text{on } \partial\Omega, \\ P_\varepsilon = \frac{1}{\varepsilon}(\rho_\varepsilon - \rho_0) & \text{in } \Omega. \end{cases}$$

2.1.4 Molecular dynamics

For $t \in \mathbb{R}_+$ and $\mathbf{x} \in \Omega$, we denote by $C(t, \mathbf{x})$ the concentration of a molecular species inside the cell. It follows advection-diffusion dynamics with no-flux boundary condition, ensuring conservation of the total molecular mass M . The advection represents the active transport by the cytoskeleton following the fluid velocity field. Note that a justification of this equation for molecular transport can be found in [24]. For $t > 0$, the model writes

$$\begin{cases} \partial_t C + \operatorname{div} (C \mathbf{U} - D' \nabla C) = 0 & \text{for } \mathbf{x} \in \Omega, \\ (C \mathbf{U} - D' \nabla C) \cdot \mathbf{n} = 0 & \text{for } \mathbf{x} \in \partial\Omega, \end{cases}$$

where D' is the diffusion coefficient, with $D' \geq \underline{D}'$ for some $\underline{D}' > 0$.

Finally, we assume activated molecules at the cell boundary are able to inhibit actin polymerisation: K_p is an increasing function of the molecular concentration. A typical formulation involves a Hill function, and writes $K_p(C(t, \mathbf{x})) = \bar{k}C(t, \mathbf{x})/(c_t + C(t, \mathbf{x}))$, where $\bar{k}, c_t > 0$.

2.2 Formal derivation of the reduced model

2.2.1 Non-dimensionalization

The non-dimensionalization of the problem is based on the following typical quantities:

$$\begin{aligned} \bar{L} &= R, & \bar{T} &= K_d^{-1}, & \bar{V} &= \frac{\bar{L}}{\bar{T}} = RK_d, \\ \bar{F} &= \xi \bar{V} = \xi RK_d, & \bar{P} &= \bar{F} \bar{L} = \xi R^2 K_d, & \bar{C} &= M. \end{aligned}$$

The dimensionless equations are now written using lower case letters for the dimensionless variables and keeping the notation ε for simplicity. Let $\Omega := B(0, 1)$ be the unit disk representing the cell domain. Then, the Stokes Problem rewrites

$$\begin{cases} -\tilde{\eta} \Delta \mathbf{u} + \nabla p = -(\mathbf{u} + \mathbf{v}) & \text{in } \Omega, \\ \tilde{\eta} (\nabla \mathbf{u} + {}^t \nabla \mathbf{u}) \cdot \mathbf{n} - p \mathbf{n} = \chi k_p(c) \mathbf{n} & \text{on } \partial\Omega, \end{cases}$$

with $\tilde{\eta} := \frac{\eta}{\xi R^2}$, $\chi := \frac{\bar{k}}{\bar{P}}$, and $k_p(c) = \frac{c}{c_t + c}$ in the typical case. The continuity equation rewrites

$$\begin{cases} \frac{\partial}{\partial t} \rho_\varepsilon + \operatorname{div} (\rho_\varepsilon \mathbf{u}) = -\rho_\varepsilon & \text{in } \Omega, \\ \rho_\varepsilon = \rho_0 - \varepsilon \bar{k} k_p(c) & \text{on } \partial\Omega, \\ \bar{P} p_\varepsilon = \frac{1}{\varepsilon}(\rho_\varepsilon - \rho_0) & \text{in } \Omega. \end{cases}$$

The molecular problem now writes

$$\begin{cases} \partial_t c + \operatorname{div} (c \mathbf{u} - D \nabla c) = 0 & \text{for } \mathbf{x} \in \Omega, \\ (c \mathbf{u} - D \nabla c) \cdot \mathbf{n} = 0 & \text{for } \mathbf{x} \in \partial\Omega, \end{cases}$$

with $D := \frac{D'}{R^2 K_d}$. The cell velocity equation remains unchanged.

2.2.2 Reduction to a Darcy-Poisson problem

In the context of crawling cell migration, it is known that the friction forces associated with crawling are very large compared to the cytoskeleton viscosity [25, 26]. With that in mind, formally taking $\tilde{\eta} \rightarrow 0$ in the Stokes equation reduces to a Darcy law

$$\begin{cases} \mathbf{u}(t, \mathbf{x}) = -\nabla p(t, \mathbf{x}) - \mathbf{v}(t) & \text{in } \Omega, \\ p(t, \mathbf{x}) \mathbf{n} = -\chi k_p(c) \mathbf{n} & \text{on } \partial\Omega. \end{cases}$$

Remark 1 The Darcy law can also be obtained from a 3D Stokes problem with Dirichlet boundary conditions under an infinitesimal width assumption [8].

The continuity equation on ρ_ε combined with the Darcy law allows to write

$$\begin{aligned} \varepsilon \partial_t p_\varepsilon &= \operatorname{div} (\rho_0 (\nabla p_\varepsilon + \mathbf{v}) + \varepsilon p_\varepsilon (\nabla p_\varepsilon + \mathbf{v})) - (\rho_0 + \varepsilon p_\varepsilon) & \text{in } \Omega, \\ &= \operatorname{div} (\rho_0 \nabla p_\varepsilon + \varepsilon p_\varepsilon (\nabla p_\varepsilon + \mathbf{v})) - (\rho_0 + \varepsilon p_\varepsilon), \end{aligned}$$

since $\mathbf{v}$ does not depend on the space variable. Therefore, in the formal limit $\varepsilon \rightarrow 0$, the fluid density is constant, and the fluid pressure satisfies the following Poisson-Dirichlet problem:

$$\begin{cases} -\Delta p(t, \mathbf{x}) = -1 & \text{in } \Omega, \\ p(t, \mathbf{x}) = -\chi k_p(c(t, \mathbf{x})) & \text{on } \partial\Omega. \end{cases}$$

The boundary condition accounts for polymerisation at the edge of the cell, while the sink term -1 describes depolymerisation in the cell body. Finally, the cell velocity now writes

$$\mathbf{v}(t) = \gamma \int_{\partial\Omega} p(t, \mathbf{x}) \mathbf{n} \, d\sigma(\mathbf{x}) = -\gamma \chi \int_{\partial\Omega} k_p(c(t, \mathbf{x})) \mathbf{n} \, d\sigma(\mathbf{x}),$$

with $\gamma := \frac{\xi}{\xi_1}$ the friction ratio. This expression shows that the cell displacement follows from the boundary coupling to the molecular dynamics. The new parameters are listed below.

2.3 Discussion of model derivation

This model aims to provide a minimal description of the mechanical and chemical machinery in a single crawling cell. The model's mechanical features connect the cytoskeleton dynamics with cell displacement as follows. The non-positive Dirichlet

Non-dimensionalized parameters	
Viscosity	$\tilde{\eta} := \frac{\eta}{\xi R^2} \rightarrow 0$
Polymerisation magnitude	$\chi := \frac{\bar{k}}{\xi R^2 K_d}$
Diffusion coefficient	$D := \frac{D'}{L V} = \frac{D'}{R^2 K_d}$
Balance of frictions	$\gamma := \frac{\xi}{\xi_1}$

boundary condition on the pressure in the Poisson problem (3) accounts for polymerisation inhibition from a constant (resting) actin density value ρ_0 . This results in mostly negative pressure, with higher values at the boundary and lower depolymerisation-driven values in the cell centre, thus creating a pressure gradient directed towards the cell boundary. The actin velocity, as given by the Darcy problem (2), consists of two components. The local term is the negative pressure gradient, representing the inward actin flow caused by polymerisation dynamics. The nonlocal term is the negative cell velocity, arising from actin flow friction forces expressed in the cell's frame of reference. This acts as an additional directional bias on the actin flow resulting from the cell's own motion. Mechanical equilibrium between the cell's passive drags and fluid friction determines the cell velocity (4). Consequently, the asymmetry in the negative boundary pressure, and thus in fluid pulling, drives cell displacement. Overall, inhomogeneous polymerisation at the boundary drives polarisation of actin flows through both local and non-local effects, mediating a link between cell velocity and actin flows. This is consistent with the observation that faster cells exhibit larger actin flows. Depolymerisation has only a local depolarising effect.

The molecular species is transported by actin flows, and is responsible for inhibiting polymerisation under the pressure boundary condition. As in [4], it is described using a nonlinear Hill function to quantify instantaneous activation with saturation. The Hill coefficient is set to 1 for simplicity, as it was found to have little effect within the range [0.7, 1.5]. This leads to a cell velocity that is directly determined by integrating the boundary molecular concentration, so that faster cell velocities result from steeper concentration gradients across the cell, due to accumulation at the cell rear.

From the modelling viewpoint, the main novelty in our model lies in the Poisson problem on the fluid pressure arising from the continuity equation on actin density. Some previous fluid-based models assumed constant actin density, so that polymerisation terms were supported by the actin velocity equations [8, 9]. In [19] and subsequent works, the fluid pressure is a solution of a Laplace problem with Young-Laplace boundary condition perturbed by an active term that can model polymerisation, but no link is established with the actin density dynamics. Here, we follow [23] to define a pressure law from the actin density. Hence, in the limit of constant actin density, this yields a pressure problem describing both boundary polymerisation and bulk depolymerisation.

From the mathematical viewpoint, the key dynamics of the model is the non-local advection-diffusion equation on the molecular concentration, where the non-local term depends on boundary values. This recalls a yeast cell's polarisation model developed and studied in [27–32], where some polarity cues were actively transported towards the cell membrane by the cytoskeleton. Similar problems for cell motility have been studied in a one-dimensional setting [18, 33–35]. Other two-dimensional models were partially mathematically studied, with travelling wave solutions [17, 20, 22] and existence results [36].

3 Mathematical analysis

3.1 Some estimates for (1) – (4)

In this Subsection, we provide energy estimates for (1) – (4) for sufficiently smooth solutions. We first recall some results concerning the Dirichlet-to-Neumann operator, and then prove energy estimates using these properties.

3.1.1 The Dirichlet-to-Neumann operator

Definition 1 Let Ω be a smooth enough open set of $\mathbb{R}^2$, the Dirichlet-to-Neumann operator $\mathcal{I}_\Omega$ is defined by

$$\begin{aligned}\mathcal{I}_\Omega : H^1(\partial\Omega) &\rightarrow L^2(\partial\Omega) \\ \varphi &\rightarrow \nabla q \cdot \mathbf{n},\end{aligned}$$

where the function q denotes the harmonic extension of φ to the domain Ω , that is

$$\begin{aligned}\Delta q &= 0 \quad \text{in } \Omega, \\ q &= \varphi \quad \text{on } \partial\Omega.\end{aligned}$$

The name of this operator comes from the fact that it makes the transition between a problem verifying a Dirichlet boundary condition towards a problem with a Neumann boundary condition.

Proposition 1 Let Ω and φ be smooth enough and let q be the harmonic extension of φ , then it holds that

$$\int_{\partial\Omega} \varphi \mathcal{I}_\Omega \varphi \, d\sigma = \int_{\Omega} |\nabla q|^2 \, d\mathbf{x}.$$

Hence

$$\int_{\partial\Omega} \varphi \mathcal{I}_\Omega \varphi \, d\sigma = \inf \left\{ \int_{\Omega} |\nabla \psi|^2 \, d\mathbf{x}, \, \forall \psi \in H^1(\Omega), \, \text{s.t. } \psi = \varphi \text{ on } \partial\Omega \right\}.$$

In the case where $\Omega = B_{R_0}$ the disk of radius $R_0 > 0$, by expanding the function φ in Fourier series, it is possible to define $\mathcal{I}_{R_0} := \mathcal{I}_{B_{R_0}}$ as follows:

Definition 2 The Dirichlet-to-Neumann operator $\mathcal{I}_{R_0} : H^1(\mathbb{R}/2\pi\mathbb{Z}) \rightarrow L^2(\mathbb{R}/2\pi\mathbb{Z})$ is defined by

$$\mathcal{I}_{R_0}(\varphi)(\theta) = \sum_{n=1}^{\infty} n R_0^{n-1} (a_n \cos(n\theta) + b_n \sin(n\theta)),$$

for $\varphi(\theta) = a_0 + \sum_{n=1}^{\infty} R_0^n (a_n \cos(n\theta) + b_n \sin(n\theta))$.

This is simply because harmonic functions q on B_{R_0} write in polar coordinates for $(r, \theta) \in [0, R] \times \mathbb{R}/2\pi\mathbb{Z}$ as:

$$q(r, \theta) = \sum_{n \geq 0} a_n \cos(n\theta) r^n + b_n \sin(n\theta) r^n,$$

after discarding solutions that diverge at $r = 0$, and then

$$\nabla q(R_0, \theta) \cdot \mathbf{n} = \partial_r q(R_0, \theta) = \sum_{n \geq 1} n R_0^{n-1} (a_n \cos(n\theta) + b_n \sin(n\theta)).$$

We deduce the following Lemma.

Lemma 2 *The operator $\mathcal{I}_{R_0}$ has $R_0^{-1}\mathbb{N}^*$ as its set of eigenvalues. Furthermore, $\text{Ker}(-\mathcal{I}_{R_0} + nI_d) = \text{span}\{\cos(n\theta)\}$ has dimension 1.*

For brevity, in the sequel $\mathcal{I}_{R_0=1}$ will be simply denoted by $\mathcal{I}$, and B_1 will denote the unit disk.

3.1.2 Energy estimates

We now introduce an energy for which we provide a priori estimates.

Proposition 3 *Assume c is a solution to (1) – (4) and f is a smooth enough function on $\mathbb{R}_+$. Then, the following equality holds*

$$\begin{aligned} \frac{d}{dt} \int_{B_1} f(c) \, d\mathbf{x} &= - \int_{\partial B_1} (f(c) - cf'(c)) \mathcal{I}(\chi k_p(c)) \, d\sigma - D \int_{B_1} f''(c) |\nabla c|^2 \, d\mathbf{x} \\ &\quad - \gamma \chi \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right) \cdot \left(\int_{\partial B_1} (f(c) - cf'(c)) \mathbf{n} \, d\sigma \right) \\ &\quad + \frac{1}{2} \int_{B_1} \begin{pmatrix} x \\ y \end{pmatrix} \cdot \nabla (f(c) - cf'(c)) \, d\mathbf{x}. \end{aligned}$$

Proof We first see that

$$\frac{d}{dt} \int_{B_1} f(c) \, d\mathbf{x} = \int_{B_1} f'(c) \, \text{div} (D \nabla c - c \mathbf{u}) \, d\mathbf{x}.$$

Then, we have that

$$\begin{aligned}
\int_{B_1} f'(c) \operatorname{div} (c \mathbf{u}) \, d\mathbf{x} &= - \int_{B_1} c f'(c) \, d\mathbf{x} - \int_{B_1} \nabla f(c) \nabla p \, d\mathbf{x} \\
&\quad + \gamma \chi \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right) \left(\int_{B_1} \nabla f(c) \, d\mathbf{x} \right) \\
&= \int_{B_1} (f(c) - c f'(c)) \, d\mathbf{x} - \int_{\partial B_1} f(c) \nabla p \cdot \mathbf{n} \, d\sigma \\
&\quad + \gamma \chi \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right) \cdot \left(\int_{\partial B_1} f(c) \mathbf{n} \, d\sigma \right).
\end{aligned}$$

On the other hand, using the boundary condition in (1), we have that

$$\begin{aligned}
D \int_{B_1} f'(c) \Delta c \, d\mathbf{x} &= -D \int_{B_1} f''(c) |\nabla c|^2 \, d\mathbf{x} + D \int_{\partial B_1} f'(c) \nabla c \cdot \mathbf{n} \, d\sigma \\
&= -D \int_{B_1} f''(c) |\nabla c|^2 \, d\mathbf{x} - \int_{\partial B_1} c f'(c) \nabla p \cdot \mathbf{n} \, d\sigma \\
&\quad + \gamma \chi \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right) \cdot \left(\int_{\partial B_1} c f'(c) \mathbf{n} \, d\sigma \right),
\end{aligned}$$

which leads to

$$\begin{aligned}
\frac{d}{dt} \int_{B_1} f(c) \, d\mathbf{x} &= -\gamma \chi \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right) \cdot \left(\int_{\partial B_1} (f(c) - c f'(c)) \mathbf{n} \, d\sigma \right) \\
&\quad - D \int_{B_1} f''(c) |\nabla c|^2 \, d\mathbf{x} + \int_{\partial B_1} (f(c) - c f'(c)) \nabla p \cdot \mathbf{n} \, d\sigma \\
&\quad - \int_{B_1} (f(c) - c f'(c)) \, d\mathbf{x}.
\end{aligned}$$

Moreover, defining $\bar{p}$ in B_1 such that $\bar{p}(t, \mathbf{x}) := p(t, \mathbf{x}) - \frac{1}{4} \|\mathbf{x}\|_2^2$, we obtain that for any smooth function g on R_+ ,

$$\begin{aligned}
\int_{\partial B_1} g(c) \nabla p \cdot \mathbf{n} \, d\sigma &= \int_{\partial B_1} g(c) \nabla \bar{p} \cdot \mathbf{n} \, d\sigma + \frac{1}{2} \int_{\partial B_1} g(c) \begin{pmatrix} x \\ y \end{pmatrix} \cdot \mathbf{n} \, d\sigma \\
&= - \int_{\partial B_1} g(c) \mathcal{I} \left(\chi k_p(c) + \frac{1}{4} \right) \, d\sigma + \frac{1}{2} \int_{\partial B_1} g(c) \begin{pmatrix} x \\ y \end{pmatrix} \cdot \mathbf{n} \, d\sigma.
\end{aligned}$$

Consequently,

$$\begin{aligned}
\frac{d}{dt} \int_{B_1} f(c) \, d\mathbf{x} &= -\gamma \chi \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right) \cdot \left(\int_{\partial B_1} (f(c) - c f'(c)) \mathbf{n} \, d\sigma \right) \\
&\quad - D \int_{B_1} f''(c) |\nabla c|^2 \, d\mathbf{x} - \int_{\partial B_1} (f(c) - c f'(c)) \mathcal{I} \left(\chi k_p(c) + \frac{1}{4} \right) \, d\sigma \\
&\quad + \frac{1}{2} \int_{\partial B_1} (f(c) - c f'(c)) \begin{pmatrix} x \\ y \end{pmatrix} \cdot \mathbf{n} \, d\sigma - \int_{B_1} (f(c) - c f'(c)) \, d\mathbf{x}, \\
&= -\gamma \chi \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right) \cdot \left(\int_{\partial B_1} (f(c) - c f'(c)) \mathbf{n} \, d\sigma \right) \\
&\quad - D \int_{B_1} f''(c) |\nabla c|^2 \, d\mathbf{x} - \int_{\partial B_1} (f(c) - c f'(c)) \mathcal{I} (\chi k_p(c)) \, d\sigma \\
&\quad + \frac{1}{2} \int_{B_1} \nabla (f(c) - c f'(c)) \cdot \begin{pmatrix} x \\ y \end{pmatrix} \, d\mathbf{x},
\end{aligned}$$

by integration by part, and because $\mathcal{I}(\frac{1}{4}) = 0$ from Definition 2. □

Next, considering a particular function f yields the following estimation.

Proposition 4 *Assume that*

$$f(c) - cf'(c) = -\chi k_p(c). \quad (6)$$

Then,

1. Any H^1 solution to (1) – (4) satisfies

$$\begin{aligned} \frac{d}{dt} \int_{B_1} f(c) \, d\mathbf{x} &\leq - \int_{B_1} \left(Df''(c) - \chi^2 \left(1 + \frac{1}{4} + \gamma\pi \right) |k'_p(c)|^2 \right) |\nabla c|^2 \, d\mathbf{x} \\ &\quad + \frac{\pi}{4}. \end{aligned} \quad (7)$$

2. If it holds additionally that

$$Df''(c) \geq \chi^2 \left(1 + \frac{1}{4} + \gamma\pi \right) |k'_p(c)|^2, \quad (8)$$

then

$$\frac{d}{dt} \int_{B_1} f(c) \, d\mathbf{x} \leq \frac{\pi}{4}.$$

Proof Consider a function f such that Equation (6) holds. Then, Proposition 3 rewrites

$$\begin{aligned} \frac{d}{dt} \int_{B_1} f(c) \, d\mathbf{x} &= \gamma\chi^2 \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right)^2 - D \int_{B_1} f''(c) |\nabla c|^2 \, d\mathbf{x} \\ &\quad + \chi^2 \int_{\partial B_1} k_p(c) \mathcal{I}(k_p(c)) \, d\sigma - \frac{\chi}{2} \int_{B_1} \nabla k_p(c) \cdot \begin{pmatrix} x \\ y \end{pmatrix} \, d\mathbf{x}, \end{aligned}$$

From Proposition 1, we obtain that

$$\begin{aligned} \int_{\partial B_1} k_p(c) \mathcal{I}(k_p(c)) \, d\sigma &\leq \int_{B_1} |\nabla k_p(c)|^2 \, d\mathbf{x} \\ &\leq \int_{B_1} |k'_p(c)|^2 |\nabla c|^2 \, d\mathbf{x}. \end{aligned}$$

The Cauchy-Schwarz inequality yields

$$\begin{aligned} \left(\int_{\partial B_1} k_p(c) \mathbf{n} \, d\sigma \right)^2 &= \left(\int_{B_1} \nabla k_p(c) \, d\mathbf{x} \right)^2 \\ &\leq \pi \int_{B_1} |k'_p(c)|^2 |\nabla c|^2 \, d\mathbf{x}. \end{aligned}$$

Finally, using Young's inequality we see that

$$\left| \frac{\chi}{2} \int_{B_1} \nabla k_p(c) \cdot \begin{pmatrix} x \\ y \end{pmatrix} \, d\mathbf{x} \right| \leq \frac{\pi}{8} + \frac{\chi^2}{4} \int_{B_1} |k'_p(c)|^2 |\nabla c|^2 \, d\mathbf{x}.$$

Hence, the Inequality (7) follows. The point 2 easily follows provided that (8) is true. □

Remark 2 One can easily solve Equation (6): for $c \geq 0$ and $a \in \mathbb{R}$, a solution f is given by

$$f(c) = ac + \chi c \int_1^c \frac{1}{z^2} k_p(z) dz.$$

Indeed, when c goes to 0, it can be shown that $\lim_{c \rightarrow 0} c \int_1^c \frac{1}{z^2} k_p(z) dz = 0$, using a double integration by parts, and the fact that k_p'' is bounded on e.g $[0, 1]$. As a consequence:

- for $k_p(c) = c$, then $k_p'(c) = 1$ and one has $f(c) = ac + \chi c \ln(c)$, so that $f''(c) = \chi c^{-1}$, and Equation (8) rewrites $D\chi c^{-1} \geq \chi^2(1.25 + \gamma\pi)$, which holds for all $c > 0$ only for $\chi = 0$.
- for $k_p(c) = \frac{c}{c_t + c}$, one has $k_p'(c) = \frac{c_t}{(c_t + c)^2}$, $f(c) = a + c_t^{-1} \chi c \ln\left(\frac{(c_t + 1)c}{c_t + c}\right)$ so that $f''(c) = \frac{\chi}{c} \left(1 - \frac{c}{(c_t + c)^2}\right)$, and Equation (8) rewrites $D\chi(c_t + c)^2 \left(2c_t + \frac{c_t^2}{c}\right) \geq \chi^2(1.25 + \gamma\pi)c_t^2$. One can find non null parameter values such that this inequality holds for all $c > 0$.

Finally, we consider the particular case where k_p is given by Equation (5) and we define the critical value χ_c by

$$\chi_c := \frac{4D}{c_t(1 + \frac{1}{4} + \gamma\pi)}. \quad (9)$$

Proposition 5 Assume k_p is given by (5) and $\chi \leq \chi_c$. Let c belong to $H^1 \cap L \log L$ be a solution to (1) – (4), then

$$\frac{d}{dt} \int_{B_1} c \log\left(\frac{c}{1+c}\right) dx \leq \frac{\pi}{8}.$$

Proof In such a case, let f be such that Equation (6) is verified. Then, for $x > 0$, one has

$$f''(x) = \chi \frac{k_p'(x)}{x} = \chi \frac{c_t}{x(c_t + x)^2},$$

and it follows that

$$f(x) = A_1 + A_2 x + \chi c_t^{-1} x \log\left(\frac{x}{c_t + x}\right),$$

for $A_1, A_2 \in \mathbb{R}$. Then, Condition (8) rewrites

$$\chi(1 + \frac{1}{4} + \gamma\pi)c_t \frac{x}{(1+x)^2} \leq D, \quad \forall x > 0. \quad (10)$$

Since $\frac{x}{(1+x)^2} \leq \frac{1}{4}$, for all $x \geq 0$, a sufficient condition for (10) to be true is $\chi \leq \chi_c$, hence the result. $\square$

3.2 Analysis of the stationary problem associated with (1) – (4)

In this Subsection, we study the stationary problem associated with (1) – (4) in $\Omega = B(0, 1)$, which reads

$$\begin{cases} \operatorname{div}(\mathbf{c}\mathbf{u} - D\nabla c) = 0 & \text{in } \Omega, \\ (D\nabla c - \mathbf{c}\mathbf{u}) \cdot \mathbf{n} = 0 & \text{on } \partial\Omega, \end{cases} \quad (11)$$

with

$$\mathbf{u}(\mathbf{x}) = -\nabla p(\mathbf{x}) - \mathbf{v} \quad \text{in } \Omega, \quad (12)$$

and

$$\begin{cases} \Delta p = 1 & \text{in } \Omega, \\ p = -\chi k_p(c) & \text{on } \partial\Omega. \end{cases} \quad (13)$$

The stationary cell velocity is

$$\mathbf{v} = \gamma \int_{\partial\Omega} p \mathbf{n} \, d\sigma = -\gamma \chi \int_{\partial\Omega} k_p(c) \mathbf{n} \, d\sigma. \quad (14)$$

In Subsubsection 3.2.1, we prove two preliminary lemmas. In Subsubsection 3.2.2, we investigate the existence and uniqueness of a resting stationary state associated with a null cell velocity ($\mathbf{v} = 0$). In Subsubsection 3.2.3, we provide conditions under which this stationary solution is linearly stable. Finally, in Subsubsection 3.2.4, we prove the existence of a one-parameter family of travelling stationary solutions.

3.2.1 Preliminary lemmas

The first Lemma gives the solution of an auxiliary Laplace-Dirichlet problem involved in the pressure. For a given function c , the function defined by $p_0(x, y) := p(x, y) - \frac{1}{4}(x^2 + y^2)$ with p solution of Problem (13), is such that

$$\begin{cases} \Delta p_0(x, y) = 0, & \text{in } \Omega \\ p_0 = -\frac{1}{4} - \chi k_p(c), & \text{on } \partial\Omega, \end{cases} \quad (15)$$

which rewrites in polar coordinates, keeping the same notations $c(r, \theta)$ and $p_0(r, \theta)$, as

$$\begin{cases} -\partial_r(r \partial_r p_0) - \frac{1}{r} \partial_\theta^2 p_0 = 0, & \text{in } (0, 1) \times (0, 2\pi), \\ p_0(1, \theta) = -\frac{1}{4} - \chi k_p(c(1, \theta)) & \text{on } (0, 2\pi). \end{cases} \quad (16)$$

We have the following classical lemma:

Lemma 6 *The unique solution of (16) in $B(0, R)$, $R > 0$, writes in integral form as*

$$p_0(r, \theta) = -\frac{1}{2\pi R} \int_0^{2\pi R} \left(\frac{1}{4} + \chi k_p(c(R, s)) \right) \frac{R^2 - r^2}{R^2 - 2rR \cos(\frac{s}{R} - \theta) + r^2} \, ds, \quad (17)$$

and its Fourier expansion writes

$$\begin{aligned} p_0(r, \theta) &= \frac{a_0}{2} + \sum_{n \geq 1} r^n (a_n \cos(n\theta) + b_n \sin(n\theta)), \quad \text{with} \\ a_0 &= -\frac{1}{\pi} \int_{-\pi}^{\pi} \left(\frac{1}{4} + \chi k_p(c(R, \theta')) \right) \, d\theta', \\ a_n &= -\frac{1}{\pi} \int_{-\pi}^{\pi} \left(\frac{1}{4} + \chi k_p(c(R, \theta')) \right) \cos(n\theta') \, d\theta', \, n \geq 1, \\ b_n &= -\frac{1}{\pi} \int_{-\pi}^{\pi} \left(\frac{1}{4} + \chi k_p(c(R, \theta')) \right) \sin(n\theta') \, d\theta', \, n \geq 1. \end{aligned} \quad (18)$$

The second lemma gives the general expression of the solutions c of (11) – (12) for given pressure p and velocity $\mathbf{v}$.

Lemma 7 *For a given function p , and a given $\mathbf{v} \in \mathbb{R}$, any nonnegative solution of (11) – (12) is given by*

$$c(x, y) = c_0 e^{-\frac{p(x, y) + \mathbf{v} \cdot (x, y)^T}{D}}, \quad (x, y) \in \Omega, \quad (19)$$

where $c_0 > 0$.

Proof Indeed, it is straightforward that $c(x, y) = e^{-\frac{p(x, y) + \mathbf{v} \cdot (x, y)^T}{D}}$ is a solution of (11) – (12). Let us prove its uniqueness up to a multiplicative constant. Indeed, for an unknown function $\tilde{c}$, write

$$c(x, y) = \tilde{c}(x, y) e^{-\frac{p(x, y) + \mathbf{v} \cdot (x, y)^T}{D}}.$$

Then, $\tilde{c}$ satisfies a Laplace equation with Neumann boundary conditions given by

$$\begin{cases} \Delta \tilde{c} = 0 & \text{in } \Omega, \\ \nabla \tilde{c} \cdot \mathbf{n} = 0 & \text{on } \partial\Omega. \end{cases} \quad (20)$$

Since Ω is smooth enough (*e.g.* $\partial\Omega$ is of class $\mathcal{C}^2$), the maximum principle yields that $\tilde{c} \equiv c_0$ constant in Ω . $\square$

3.2.2 Existence and uniqueness of the rest state

Let us define

$$\chi_0 := \frac{D}{A}, \quad (21)$$

where A is given by (A3). We now prove that there exists a unique resting stationary state for (1) – (4).

Proposition 8 (Radially symmetric stationary solution) *Assume that k_p satisfies Assumption A1. Then, for all $\gamma, D, \chi > 0$, there exists a stationary solution to (1) – (4) such that $\mathbf{v} = 0$. It is given in polar coordinates for $r \in [0, 1]$ by*

$$\bar{c}(r) = c^* e^{\frac{1}{4D}(1-r^2)}, \quad (22)$$

with

$$c^* := \frac{1}{4\pi D \left(e^{\frac{1}{4D}} - 1 \right)}. \quad (23)$$

If additionally k_p satisfies Assumption A3. and $\chi \in (0, \chi_0)$, it is the unique resting stationary solution.

Proof The proof is divided in two steps. First, we show that for a given boundary value for c , there exists a unique axisymmetric solution c . Then, we consider the fully coupled system and prove uniqueness of the solution.

Let us assume that c is axisymmetric, so that $c|_{\partial\Omega} = c^*$ for some $c^* > 0$. Using Lemma 6, we deduce from Equation (18) that only a_0 is nonzero, so that

$$p(r, \theta) = \frac{1}{4}(r^2 - 1) - \chi k_p(c^*). \quad (24)$$

By the axisymmetric assumption on c , Equation (14) yields that $\mathbf{v} = 0$, hence

$$u(r, \theta) = -\partial_r p \vec{e}_r - \frac{1}{r} \partial_\theta p \vec{e}_\theta = -\frac{1}{2} r \vec{e}_r. \quad (25)$$

The polar problem associated with (11) writes

$$\begin{cases} \partial_r(r(cu_r - D\partial_r c)) + \partial_\theta(cu_\theta - D\partial_\theta c) = 0, & \text{for } r < 1, \\ (cu_r - D\partial_r c) = 0, & \text{for } r = 1. \end{cases} \quad (26)$$

Since $u_\theta = 0$ and the boundary value c^* is constant, it is clear that the solution is axisymmetric ($\partial_\theta c = 0$). We write now $c(r)$ for the unknown, and the corresponding problem rewrites

$$\begin{cases} \partial_r(\frac{1}{2}r^2 c + Dr\partial_r c) = 0, & \text{for } r < 1, \\ \frac{1}{2}rc + D\partial_r c = 0, & \text{for } r = 1, \\ c = c^*, & \text{for } r = 1. \end{cases} \quad (27)$$

The first equation can be written

$$Dr\partial_r^2 c + \left(D + \frac{1}{2}r^2\right)\partial_r c + rc = 0. \quad (28)$$

For $0 < r \leq 1$, the solutions of this equation form a bidimensional space. One solution is given by

$$c_1(r) = c^* e^{\frac{1}{4D}(1-r^2)}, \text{ with } c^* = \frac{1}{4\pi D(e^{\frac{1}{4D}} - 1)},$$

since

$$\int_0^1 c^* e^{\frac{1}{4D}(1-r^2)} r \, dr = \frac{1}{2\pi}.$$

The Wronskian associated with the second order ODE is computed to find another solution c_2 such that $\{c_1, c_2\}$ forms a basis of the space of solutions. The Wronskian W is a solution of

$$W'(r) = -\frac{D + \frac{1}{2}r^2}{Dr} W(r) = -\left(\frac{1}{r} + \frac{1}{2D}r\right) W(r). \quad (29)$$

The solution writes

$$W(r) = W(1) \frac{1}{r} e^{\frac{1}{4D}(1-r^2)}. \quad (30)$$

Moreover, we have $W(r) = c_1(r)c_2'(r) - c_2(r)c_1'(r)$, leading to the following ODE on c_2 :

$$c_2'(r) + \frac{1}{2D}rc_2(r) = \frac{W(1)}{c^*r}, \quad (31)$$

A simple computation shows that c_2 satisfies the boundary condition in Problem (27) if and only if $W(1) = 0$, leading to $c_2 = c_1$. Therefore, for any given boundary value $c^* > 0$, the unique axisymmetric stationary solution is given by Equation (22).

Now consider the fully coupled problem. Lemma 7 provides the general expression of c , so that for $\mathbf{v} = 0$, we have the following Poisson-Dirichlet problem:

$$\begin{cases} \Delta p = 1 & \text{in } \Omega, \\ p = -\chi k_p\left(c_0 e^{-\frac{p}{B}}\right) & \text{on } \partial\Omega, \end{cases} \quad (32)$$

where c_0 is a positive constant. Uniqueness of a solution follows from uniqueness of a pressure value satisfying the boundary condition. Let us define the function g in $\mathbb{R}$ by

$$g(x) := x + \chi k_p \left(c_0 e^{-\frac{x}{D}} \right),$$

so that

$$g'(x) = 1 - \frac{\chi}{D} c_0 e^{-\frac{x}{D}} k_p' \left(c_0 e^{-\frac{x}{D}} \right).$$

Therefore, from Assumption A3. together with $\chi < \chi_0 = \frac{D}{A}$, we obtain that g is increasing. Hence, there exists a unique negative root of g . This proves the uniqueness of the solution to (32). $\square$

In the case where k_p is given by Equation (5), the following corollary follows.

Corollary 9 *Assume that the function k_p is given by (5) and that $\chi < \chi_0 = 4D$. Then, there exists a unique stationary solution to (1) – (4) such that $\mathbf{v} = 0$ and it is given by Equation (22).*

Proof The proof follows from the inequality $\frac{x}{(c_t+x)^2} \leq \frac{1}{4}$ for all $x \geq 0$. $\square$

3.2.3 Linear stability analysis of the radially symmetric stationary solution for (1) – (4)

Let us consider a radially symmetric reference stationary solution $(\bar{c}, \bar{p})$ where $\bar{c}$ is given by Equation (22) and $\bar{p}$ is solution of

$$\begin{cases} -\Delta \bar{p} = -1 & \text{in } \Omega, \\ \bar{p} = -\chi k_p(\bar{c}) & \text{on } \partial\Omega. \end{cases}$$

Then, linearizing Problem (1) – (4) around $(\bar{c}, \bar{p})$, and writing

$$c = \bar{c} + \varepsilon \tilde{c} + \text{h.o.t.}, \quad p = \bar{p} + \varepsilon \tilde{p} + \text{h.o.t.},$$

one can get the following problem for $\tilde{c}$ and $\tilde{p}$:

$$\begin{cases} \partial_t \tilde{c} = \operatorname{div} (D \nabla \tilde{c} + \tilde{c} \nabla \bar{p} + \bar{c} \nabla \tilde{p} + \gamma \bar{c} \int_{\partial\Omega} \tilde{p} \mathbf{n} d\sigma) & \text{in } \Omega, \\ (D \nabla \tilde{c} + \tilde{c} \nabla \bar{p} + \bar{c} \nabla \tilde{p} + \gamma \bar{c} \int_{\partial\Omega} \tilde{p} \mathbf{n} d\sigma) \cdot \mathbf{n} = 0 & \text{on } \partial\Omega, \end{cases} \quad (33)$$

and

$$\begin{cases} -\Delta \tilde{p} = 0 & \text{in } \Omega, \\ \tilde{p} = -\chi k_p'(\bar{c}) \tilde{c} & \text{on } \partial\Omega. \end{cases}$$

Some estimates on $\tilde{c}$ and $\tilde{p}$ can be obtained. First, the mass constraint on c and $\bar{c}$ yields $\int_{\Omega} \tilde{c} d\mathbf{x} = 0$, and the Poincaré inequality gives

$$\int_{\Omega} \tilde{c}^2 d\mathbf{x} \leq \left(\frac{2}{\pi} \right)^2 \int_{\Omega} |\nabla \tilde{c}|^2 d\mathbf{x}.$$

Furthermore, since the harmonic extension minimizes the Dirichlet energy for a fixed boundary data, we have

$$\int_{\Omega} |\nabla \tilde{p}|^2 d\mathbf{x} \leq \chi^2 (k'_p(c^*))^2 \int_{\Omega} |\nabla \tilde{c}|^2 d\mathbf{x}. \quad (34)$$

Finally, let us define

$$\chi_1 := \frac{4\pi D(1 - e^{-\frac{1}{4D}})(D - \frac{1}{\pi})}{(1 + \gamma\pi) |k'_p(c^*)|}. \quad (35)$$

We can prove the following Proposition.

Proposition 10 (Linear stability) *Assume that k_p satisfies assumptions A1.-A2. and that $\chi < \chi_1$. Then, the radially symmetric reference stationary solution $\tilde{c}$ given by (23)–(22) is linearly stable.*

Proof We first see that

$$\begin{aligned} \frac{d}{dt} \int_{\Omega} |\tilde{c}|^2 d\mathbf{x} &= \int_{\Omega} \tilde{c} \operatorname{div} \left(D \nabla \tilde{c} + \tilde{c} \nabla \bar{p} + \tilde{c} \nabla \tilde{p} + \gamma \tilde{c}(\mathbf{x}) \int_{\partial\Omega} \tilde{p}(t, \mathbf{x}) \mathbf{n} d\sigma \right) d\mathbf{x} \\ &= -D \int_{\Omega} |\nabla \tilde{c}|^2 d\mathbf{x} - \int_{\Omega} \tilde{c} \nabla \tilde{c} \cdot \nabla \bar{p} d\mathbf{x} - \int_{\Omega} \tilde{c} \nabla \tilde{c} \cdot \nabla \tilde{p} d\mathbf{x} \\ &\quad - \gamma \int_{\Omega} \tilde{c}(\mathbf{x}) \nabla \tilde{c}(t, \mathbf{x}) d\mathbf{x} \int_{\partial\Omega} \tilde{p}(t, \mathbf{x}) \mathbf{n} d\sigma. \end{aligned}$$

Using the Poincaré inequality, we obtain

$$\begin{aligned} \left| \int_{\Omega} \tilde{c} \nabla \tilde{c} \cdot \nabla \bar{p} d\mathbf{x} \right| &\leq \|\nabla \bar{p}\|_{L^\infty(\Omega)} \left(\int_{\Omega} |\nabla \tilde{c}|^2 d\mathbf{x} \right)^{1/2} \left(\int_{\Omega} |\tilde{c}|^2 d\mathbf{x} \right)^{1/2} \\ &\leq \frac{2}{\pi} \|\nabla \bar{p}\|_{L^\infty(\Omega)} \int_{\Omega} |\nabla \tilde{c}|^2 d\mathbf{x}. \end{aligned}$$

Furthermore, using (34), we have

$$\begin{aligned} \left| \int_{\Omega} \tilde{c} \nabla \tilde{c} \cdot \nabla \tilde{p} d\mathbf{x} \right| &\leq \|\tilde{c}\|_{L^\infty(\Omega)} \int_{\Omega} |\nabla \tilde{c} \cdot \nabla \tilde{p}| d\mathbf{x} \\ &\leq \|\tilde{c}\|_{L^\infty(\Omega)} \left(\int_{\Omega} |\nabla \tilde{c}|^2 d\mathbf{x} \right)^{1/2} \left(\int_{\Omega} |\nabla \tilde{p}|^2 d\mathbf{x} \right)^{1/2} \\ &\leq \chi |k'_p(c^*)| \|\tilde{c}\|_{L^\infty(\Omega)} \int_{\Omega} |\nabla \tilde{c}|^2 d\mathbf{x}. \end{aligned}$$

Finally, since

$$\begin{aligned} -\gamma \int_{\Omega} \tilde{c} \nabla \tilde{c} d\mathbf{x} \int_{\partial\Omega} \tilde{p} \mathbf{n} d\sigma &= \gamma \chi k'_p(c^*) \int_{\Omega} \tilde{c} \nabla \tilde{c} d\mathbf{x} \int_{\partial\Omega} \tilde{c} \mathbf{n} d\sigma \\ &= \gamma \chi k'_p(c^*) \int_{\Omega} \tilde{c} \nabla \tilde{c} d\mathbf{x} \int_{\Omega} \nabla \tilde{c} d\mathbf{x}, \end{aligned}$$

and

$$\gamma \chi k'_p(c^*) \int_{\Omega} \tilde{c} \nabla \tilde{c} d\mathbf{x} \leq \gamma \chi |k'_p(c^*)| \|\tilde{c}\|_{L^\infty(\Omega)} \int_{\Omega} |\nabla \tilde{c}| d\mathbf{x},$$

it holds that

$$-\gamma \int_{\Omega} \bar{c} \nabla \tilde{c} \, d\mathbf{x} \int_{\partial\Omega} \tilde{p} \, d\sigma \leq \gamma \chi \pi |k'_p(c^*)| \|\bar{c}\|_{L^\infty(\Omega)} \int_{\Omega} |\nabla \tilde{c}|^2 \, d\mathbf{x}.$$

Consequently, we have

$$\begin{aligned} & \frac{d}{dt} \int_{\Omega} |\tilde{c}|^2 \, d\mathbf{x} \\ & \leq - \left(D - \chi (1 + \gamma \pi) |k'_p(c^*)| \|\bar{c}\|_{L^\infty(\Omega)} - \frac{2}{\pi} \|\nabla \bar{p}\|_{L^\infty(\Omega)} \right) \int_{\Omega} |\nabla \tilde{c}|^2 \, d\mathbf{x}. \end{aligned}$$

Using Equations (22) and (24), we deduce that

$$\|\bar{c}\|_{L^\infty(\Omega)} = c^* e^{\frac{1}{4D}} = \left(4\pi D \left(1 - e^{-\frac{1}{4D}} \right) \right)^{-1},$$

together with $\|\nabla \bar{p}\|_{L^\infty(\Omega)} = \frac{1}{2}$. Moreover, Assumption A2. ensures that $|k'_p(c^*)| > 0$. Finally, a sufficient condition for linear stability is that

$$D - \chi (1 + \gamma \pi) |k'_p(c^*)| \left(4\pi D \left(1 - e^{-\frac{1}{4D}} \right) \right)^{-1} - \frac{1}{\pi} > 0,$$

from which the result follows. $\square$

In the particular case of Equation (5), we obtain a sufficient condition for the linear stability of the rest state. Let us define

$$\bar{\chi}_1 := \frac{4(\pi D - 1)e^{\frac{1}{4D}}}{\pi(1 + \gamma \pi)}. \quad (36)$$

Corollary 11 *In the case where k_p is given by Equation (5), a sufficient condition for the linear stability of the rest state is that $\chi < \bar{\chi}_1$.*

Proof The result follows from Assumption A3. that yields $|k'_p(c^*)| \leq \frac{1}{4c^*}$. $\square$

3.2.4 Existence of travelling wave stationary solutions, $\mathbf{v} \neq \mathbf{0}$

Without loss of generality, we assume forward motion in the x -direction and write $\mathbf{v} = (V, 0)^T$ with $V \in \mathbb{R}_+$. Lemma 7 allows us to eliminate c from (11)–(12)–(13)–(14) and to rewrite the stationary problem with travelling wave in the following concise form:

$$\begin{cases} -\Delta p = -1 & \text{in } \Omega_0, \\ p(1, \theta) = -\chi k_p \left(c_0 e^{-\frac{p(1, \theta) + V \cos(\theta)}{D}} \right) & \text{on } \partial\Omega, \end{cases} \quad (37)$$

together with

$$V = -\gamma \chi \int_0^{2\pi} k_p \left(c_0 e^{-\frac{p(1, \theta) + V \cos(\theta)}{D}} \right) \cos(\theta) \, d\theta, \quad (38)$$

where $\int_{\Omega} c(x, y) \, dx \, dy = 1$, leading to

$$c_0 = \frac{1}{\int_{\Omega} e^{-\frac{p(x, y) + xV}{D}} \, dx \, dy}. \quad (39)$$

Finally, for $\chi \in (0, \chi_0)$ and $D > 0$, let us define

$$\gamma_c(\chi, D) := \pi^{-1} \left[\left(\frac{\chi}{D} c^* e^{\frac{\chi}{D} k_p(c^*)} k_p' \left(c^* e^{\frac{\chi}{D} k_p(c^*)} \right) \right)^{-1} - 1 \right]. \quad (40)$$

We prove the following bifurcation result.

Proposition 12 (Bifurcation of travelling wave solutions) *Assume that k_p satisfies Assumptions A1.-A2.-A3., fix $\chi \in (0, \chi_0)$ and $D > 0$, and let $\gamma_c = \gamma_c(\chi, D)$ be defined by (40). Then there exist $V_0 > 0$ and a C^1 map*

$$(-V_0, V_0) \ni V \mapsto \gamma(V) \in \mathbb{R}, \quad \gamma(0) = \gamma_c,$$

such that, for every $V \in (-V_0, V_0)$, the system (1) – (4) admits a travelling stationary solution with velocity $\mathbf{v} = V \mathbf{e}_x$ if and only if $\gamma = \gamma(V)$. Moreover, this branch is non-trivial in the sense that $V \mapsto \gamma(V)$ is the unique branch of solutions of (37)–(38) bifurcating from the resting state ($V = 0, \gamma = \gamma_c$) other than the trivial branch $\{V = 0\}$.

Proof The proof proceeds in three steps. Steps 1 and 2 derive a scalar equation for the velocity and compute the derivative of its left-hand side at $V = 0$. Step 3 contains the bifurcation argument.

Step 1: reduction to a scalar equation. Consider Problem (37) for given $V \in \mathbb{R}$ and $(\chi, D) \in \mathbb{R}_+^2$. For all $\theta \in [0, 2\pi)$, consider the function

$$g_\theta(x) := x + \chi k_p \left(c_0 e^{-\frac{x+V \cos(\theta)}{D}} \right),$$

whose derivative reads

$$g'_\theta(x) = 1 - \frac{\chi c_0}{D} e^{-\frac{x+V \cos(\theta)}{D}} k_p' \left(c_0 e^{-\frac{x+V \cos(\theta)}{D}} \right).$$

By Assumption A3. together with $\chi \in (0, \chi_0)$, one has $g'_\theta > 0$, hence the existence and uniqueness of the solution $p(\cdot; V, \chi, D)$ to (37) follows with arguments similar to those given in the proof of Proposition 8. The normalisation constant $c_0 = c_0(V, \chi, D)$ is given by (39), and the regularity of k_p (Assumption A1.) ensures that both p and c_0 are C^2 in V at $V = 0$. We denote the corresponding solution by $p(r, \theta; V, \chi, D)$.

Define the function F by

$$F(V, \chi, D, \gamma) := V + \gamma \chi \int_0^{2\pi} k_p \left(c_0(V, \chi, D) e^{-\frac{p(1, \theta; V, \chi, D) + V \cos(\theta)}{D}} \right) \cos(\theta) d\theta. \quad (41)$$

For given parameters (χ, D, γ) , the existence of a travelling wave solution – that is Equation (38) – rewrites in the form

$$F(V, \chi, D, \gamma) = 0. \quad (42)$$

Step 2: computation of $\partial_V F$ at $V = 0$. We first observe that, by uniqueness in Step 1 and by symmetry of the radial profile $\bar{p}$, one has $F(0, \chi, D, \gamma) = 0$ for all $D, \gamma > 0$ and $\chi \in (0, \chi_0)$. Next, we compute

$$\partial_V F(V, \chi, D, \gamma) = 1 + \gamma \chi \int_0^{2\pi} \left(\partial_V c_0 - \frac{\partial_V p(1, \theta; V, \chi, D) + \cos(\theta)}{D} c_0 \right)$$

$$\times e^{\frac{-p(1,\theta;V,\chi,D)-V\cos(\theta)}{D}} k_p' \left(c_0 e^{\frac{-p(1,\theta;V,\chi,D)-V\cos(\theta)}{D}} \right) \cos(\theta) d\theta,$$

where $q(1,\theta;V,\chi,D) := \partial_V p(1,\theta;V,\chi,D)$ satisfies the following Laplace problem

$$\begin{cases} -\Delta q = 0 & \text{in } \Omega, \\ q(1,\theta;V,\chi,D) = -\chi \left(\partial_V c_0(V,\chi,D) - \frac{q(1,\theta;V,\chi,D) + \cos(\theta)}{D} c_0(V,\chi,D) \right) \\ \quad \times e^{\frac{-p(1,\theta;V,\chi,D)-V\cos(\theta)}{D}} k_p' \left(c_0(V,\chi,D) e^{\frac{-p(1,\theta;V,\chi,D)-V\cos(\theta)}{D}} \right) & \text{on } \partial\Omega, \end{cases}$$

hence $\tilde{q}(1,\theta;\chi,D) := q(1,\theta;V=0,\chi,D)$ satisfies

$$\begin{cases} -\Delta \tilde{q} = 0 & \text{in } \Omega, \\ \tilde{q}(1,\theta;\chi,D) = -\chi \left(\partial_V c_0(0,\chi,D) - \frac{\tilde{q}(1,\theta;\chi,D) + \cos(\theta)}{D} c^* \right) \\ \quad \times e^{\frac{-\bar{p}(1;\chi,D)}{D}} k_p' \left(c^* e^{\frac{-\bar{p}(1;\chi,D)}{D}} \right) & \text{on } \partial\Omega, \end{cases}$$

since $p(1,\theta;0,\chi,D) = \bar{p}(1;\chi,D) = -\chi k_p(c^*)$ and $c_0(0,\chi,D) = c^*(D) > 0$. Consequently, we obtain

$$\tilde{q}(1,\theta;\chi,D) = -\partial_V c_0(V=0,\chi,D) \frac{(1 - \frac{D}{c^*} B)}{B} + \frac{(1-B)}{B} \cos(\theta),$$

where

$$B := 1 - \frac{\chi}{D} c^* e^{\frac{\bar{p}(1;\chi,D)}{D}} k_p'(c^*) \in (0,1), \quad (43)$$

for $\chi \in (0,\chi_0)$. Hence,

$$\partial_V F(0,\chi,D,\gamma) = 1 - \gamma\pi \frac{1-B}{B}, \quad (44)$$

which vanishes precisely at $\gamma = \gamma_c(\chi,D)$ defined by (40).

Step 3: bifurcation argument. Since $F(0,\chi,D,\gamma) = 0$ for all γ , a direct application of the implicit function theorem to F near $(V=0, \gamma=\gamma_c)$ at a point where $\partial_V F \neq 0$ would only recover the trivial branch $\{V=0\}$. To detect non-trivial travelling waves, we factor out this trivial branch.

For (χ,D) fixed and V in a neighbourhood of 0, define

$$\tilde{F}(V,\gamma) := \int_0^1 \partial_V F(sV,\chi,D,\gamma) ds. \quad (45)$$

By the fundamental theorem of calculus and $F(0,\chi,D,\gamma) = 0$, one has $F(V,\chi,D,\gamma) = V \tilde{F}(V,\gamma)$, so that the non-trivial solutions of $F=0$ near $V=0$ coincide with the zeros of $\tilde{F}$. Since F is C^1 in (V,γ) (which follows from Assumption A1. and the smooth dependence established in Step 1), $\tilde{F}$ is also C^1 , and

$$\tilde{F}(0,\gamma) = \partial_V F(0,\chi,D,\gamma) = 1 - \gamma\pi \frac{1-B}{B}.$$

In particular, $\tilde{F}(0,\gamma_c) = 0$ and

$$\partial_\gamma \tilde{F}(0,\gamma_c) = -\pi \frac{1-B}{B} \neq 0,$$

since $B \in (0,1)$. The implicit function theorem applied to $\tilde{F}$ at $(0,\gamma_c)$ therefore yields $V_0 > 0$ and a C^1 map $V \mapsto \gamma(V)$ defined on $(-V_0, V_0)$, with $\gamma(0) = \gamma_c$, such that the zero set of $\tilde{F}$ in a neighbourhood of $(0,\gamma_c)$ is exactly the graph $\{(V,\gamma(V)) : V \in (-V_0, V_0)\}$. This gives the announced non-trivial branch of travelling wave solutions, and the uniqueness statement follows from this local description. $\square$

Remark 3 The argument above is the classical Crandall–Rabinowitz scheme for transcritical bifurcation from a trivial branch in the scalar setting, where the factorisation $F(V, \gamma) = V \tilde{F}(V, \gamma)$ replaces the more general Lyapunov–Schmidt reduction. The bifurcation curve can be locally inverted into $V = V(\gamma)$ as soon as $\gamma'(0) \neq 0$, which corresponds to a transcritical bifurcation. When $\gamma'(0) = 0$ and $\gamma''(0) \neq 0$, the bifurcation is of pitchfork type and yields, for each γ on one side of γ_c , a pair of solutions $\pm V$, consistent with the rotational symmetry of the problem.

Assume that k_p is given by Equation (5). Then,

$$\gamma_c(\chi, D) = \pi^{-1} \left[\left(\frac{\chi}{D} \frac{c_t c^* e^{\frac{\chi}{D} k_p(c^*)}}{(c_t + c^* e^{\frac{\chi}{D} k_p(c^*)})^2} \right)^{-1} - 1 \right],$$

leading to the following Corollary.

Corollary 13 *Assume that k_p is given by Equation (5), and fix $\chi \in (0, \chi_0)$ and $D > 0$. Let $c^*(D)$ be given by Equation (23) and $\gamma_c(\chi, D)$ be the bifurcation value above. Then there exist $V_0 > 0$ and a C^1 map $V \mapsto \gamma(V)$ defined on $(-V_0, V_0)$ with $\gamma(0) = \gamma_c(\chi, D)$, such that for every $V \in (-V_0, V_0)$ the system (1) – (4) admits a travelling stationary solution with $\mathbf{v} = V \mathbf{e}_x$ if and only if $\gamma = \gamma(V)$.*

Remark 4 The bifurcation point γ_c given by (40) is not always positive, and only the regime $\gamma_c > 0$ corresponds to a physically admissible branch in our model. Defining the quantity $E := \frac{\chi}{D} c^* e^{\frac{\chi}{D} k_p(c^*)} k_p'(c^*)$, it is clear that $\gamma_c > 0$ if and only if $E < 1$. When k_p is given by Equation (5), using the variable $G := c^* e^{\frac{\chi}{D} k_p(c^*)}$, a discriminant analysis yields the following result: $\gamma_c > 0$ is equivalent to

- either $\frac{\chi}{D} < 4$,
- either $\frac{\chi}{D} = 4$ and $c^*(D) \neq c_0^*(c_t) > 0$ unique solution of $x e^{4k_p(x)} = c_t$,
- either $\frac{\chi}{D} > 4$ and $c^*(D) > c_1^*(\frac{\chi}{D}, c_t)$ with $c_1^*(\frac{\chi}{D}, c_t) > 0$ unique solution of $x e^{\frac{\chi}{D} k_p(x)} = \frac{c_t}{2} \left(\frac{\chi}{D} - 2 + \sqrt{\frac{\chi}{D}(\frac{\chi}{D} - 4)} \right)$,
- or $\frac{\chi}{D} > 4$ and $c^*(D) < c_2^*(\frac{\chi}{D}, c_t)$ with $c_2^*(\frac{\chi}{D}, c_t) > 0$ unique solution of $x e^{\frac{\chi}{D} k_p(x)} = \frac{c_t}{2} \left(\frac{\chi}{D} - 2 - \sqrt{\frac{\chi}{D}(\frac{\chi}{D} - 4)} \right)$.

4 Numerical simulations of the intracellular dynamics

This Section is devoted to numerical simulations of solutions to (1)–(2)–(3)–(4), modelling single-cell intracellular dynamics when it moves on a surface without any external stimulation. The activation function k_p is defined by Equation (5), so that the results from Corollary 9, Corollary 11 and Corollary 13 hold.

In Subsection 3.2, a Gaussian stationary state (23)–(22) was introduced. Its uniqueness among resting states was shown for $\chi < \chi_0$, as well as its linear stability for

$\chi < \chi_1$. Moreover, for $\chi < \chi_0$ and $D > 0$, a non-trivial branch of travelling wave stationary solutions was shown to bifurcate from the resting state at $\gamma = \gamma_c(\chi, D)$. Here, we both illustrate the cases treated by the theoretical analysis and investigate the other settings.

This Section is organised as follows. Subsection 4.1 gives a brief account of the numerical setting. In Subsection 4.2, the case of a radially symmetric stationary state is illustrated in relation with Corollary 9 and Corollary 11. In Subsection 4.3, Corollary 13 is treated by showing convergence towards a travelling stationary state. Finally, Subsection 4.4 is devoted to the parameter spaces.

4.1 Numerical setting

The numerical resolution is performed in polar coordinates. Given the molecular concentration at the boundary, Lemma 6 provides an explicit expression for the pressure. Therefore, the discretization focuses on the advection-diffusion equation. The advection field being nonlinear, the advection is treated explicitly, while the diffusion term is treated implicitly. We use a finite volumes scheme in space. Unless indicated otherwise, parameters of the numerical setting are $\Delta t = 0.01$ and $\Delta r = \Delta \theta = \frac{2\pi}{200} \simeq 0.03$. The numerical discretization is further detailed in Appendix A.1.

For k_p given by Equation (5), the parameters under study are the molecular diffusion coefficient D , the magnitude χ of the molecular regulation of the boundary pressure, the parameter $c_t > 0$ such that $k_p(c_t) = \frac{1}{2}$, and γ the cell velocity parameter. Note that the latter arises only as a product with χ (see Equation (4)). The molecular mass is fixed with $M = 1$.

The simulations are pursued up until the system reaches a numerical stationary state, defined as the time t^N above which the ℓ^1 distance between the molecular concentration at two consecutive time steps remains lower than 10^{-10} during one numerical time unit (or equivalently Δt^{-1} time steps). Note that this criterion depends on the spatial discretization. For the parameter spaces, to reduce computational costs, the threshold is set at 10^{-6} and the space step is increased such that $\Delta \theta = \frac{2\pi}{120} \simeq 0.05$.

Two typical quantities can be used as outputs to characterise cell polarisation. The Relative Standard Deviation (RSD) is given by the perimeter-normalized ratio between the standard deviation of boundary values and their mean value. The Resultant Vector Length (RVL) is given by the norm of the normalized discretization of $\int_{\partial\Omega} c(1, \theta) \mathbf{n} d\theta$. Their formulas and a short discussion on their respective meanings can be found in Appendix A.2.

In the following, parameters are chosen as follows. For simulations illustrating stationary states (Figures 2–3–4), parameters D and χ vary, while $(\gamma, c_t) = (0.5, 1)$. For parameter spaces, $\gamma = 0.1$ is fixed, while the other parameters, when they do not vary, are such that $(\chi, c_t, D) = (1, 0.4, 0.3)$.

4.2 Resting stationary state

This Subsection aims at illustrating both the relaxation towards the radially symmetric resting stationary state given by Equation (22), and its linear stability. First, let us

consider the case of an initially polarised cell, with

$$c(0, r, \theta) = (1 - \sin(\theta))\mathbb{1}_{r>0}\mathcal{N}, \quad (46)$$

where $\mathcal{N}$ is the normalisation constant. Figure 2 illustrates the corresponding system for $D = 0.3$ and $\chi = 0.3 < \chi_0 = 1.2$. Subfigure (a) shows the initially polarised molecular concentration given by (46). Subfigure (b) shows the corresponding pressure field. The black arrows represent the associated radial and angular advection fields ($\mathbf{u}_r, \mathbf{u}_\theta$), while the red arrow shows the global cell velocity. The molecular asymmetry hence drives the pressure asymmetry from the boundary. Subfigure (c) shows the radially symmetric stationary molecular concentration, with a diffuse accumulation of molecules at the cell centre. Subfigure (d) shows the time evolution of both polarity indices that rapidly decrease to zero. We could not find other resting stationary profiles for $\chi > \chi_0$.

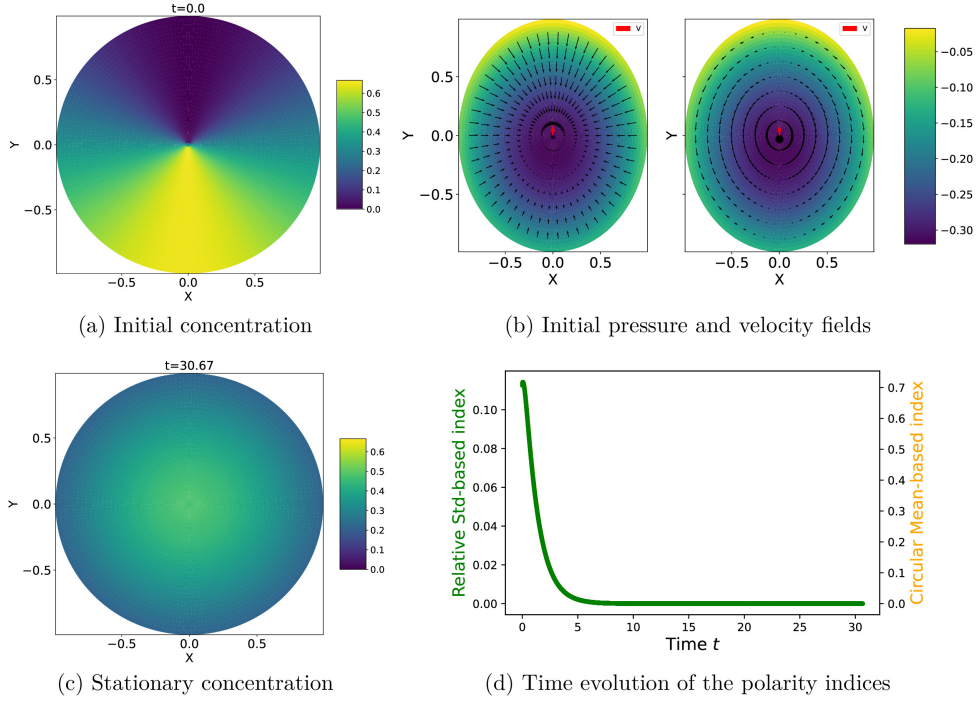


Fig. 2 Illustration of the relaxation of the system to a radially-symmetric stationary state, with $D = \chi = 0.3$ ($\chi < \chi_0$), $c_t = 1$ and $\gamma = 0.5$. (a): Polarised initial concentration given by Equation (46). (b): Initial pressure field given by Lemma 6, together with the corresponding radial (left) and angular (right) advection fields and the global cell velocity (red). (c): Stationary radially-symmetric molecular concentration. (d): Time evolution of the polarity indices (RSD in green, RVL in yellow), both curves overlap

Next, let us illustrate the linear stability of such stationary state. For that purpose, the initial condition is taken as a perturbed radially symmetric profile given by

$$c(0, r, \theta) = \bar{c}(r) + 0.1 \sin(\theta) \mathbf{1}_{r>0}, \quad (47)$$

with $\bar{c}$ given by Equations (23)–(22). Figure 3 illustrates the dynamics for $D = 0.8$ and several values for χ . In this case, the respective threshold values involved in Proposition 10 and Corollary 11 are $\chi_1 \simeq 0.82$ and $\bar{\chi}_1 \simeq 1.02$. Subfigure (a) shows the initial molecular concentration given by Equation (47). Subfigure (b) shows the stationary radial profile obtained for $\chi = 0.3 < \chi_1 < \bar{\chi}_1$ together with its analytical counterpart. Subfigure (c) shows the radially-symmetric stationary concentration obtained for $\chi = 1.85 > \bar{\chi}_1 > \chi_1$. Subfigure (d) shows the polarised stationary concentration profile obtained for $\chi = 1.9 > \bar{\chi}_1 > \chi_1$. These simulations show that the obtained theoretical thresholds are not optimal.

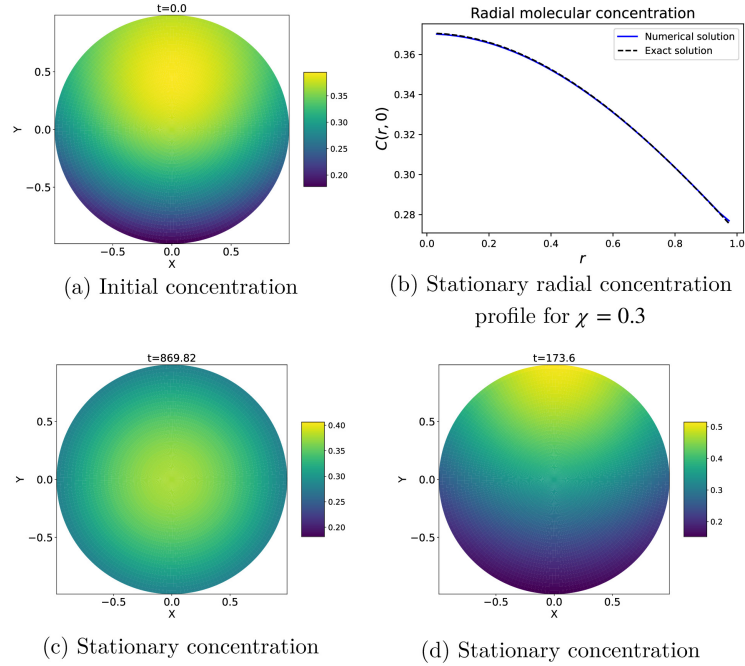


Fig. 3 Illustration of the relaxation to a radially-symmetric or polarised stationary state from a perturbed initial condition, with $D = 0.8$, $c_t = 1$ and $\gamma = 0.5$. (a): Perturbed initial concentration given by Equation (47). (b): Radial molecular profile at stationary state for $\chi = 0.3 < \chi_1 < \bar{\chi}_1$, together with the corresponding explicit solution. (c): Radially-symmetric stationary concentration obtained for $\chi = 1.85 > \bar{\chi}_1 > \chi_1$. (d): Polarised stationary concentration obtained for $\chi = 1.9 > \bar{\chi}_1 > \chi_1$.

4.3 Travelling stationary states

This Subsection aims at illustrating the numerical convergence of the system towards a travelling stationary state. The initial concentration is given by Equation (46). Figure 4 illustrates the corresponding system for $D = 0.3$ and $\chi = 1 < \chi_0 = 1.2$, with $\gamma = 0.5$ chosen so as to lie on the bifurcated branch of polarised solutions. Subfigure (a) shows the initially polarised molecular concentration given by (46). Subfigure (b) shows the corresponding pressure field. Subfigure (c) shows the polarised stationary molecular concentration, with accumulation of molecules at a part of the boundary, thus defining the cell rear. Subfigure (d) shows the time evolution of both polarity indices that grow towards a stationary value. We did not find significantly different profiles for $\chi > \chi_0$.

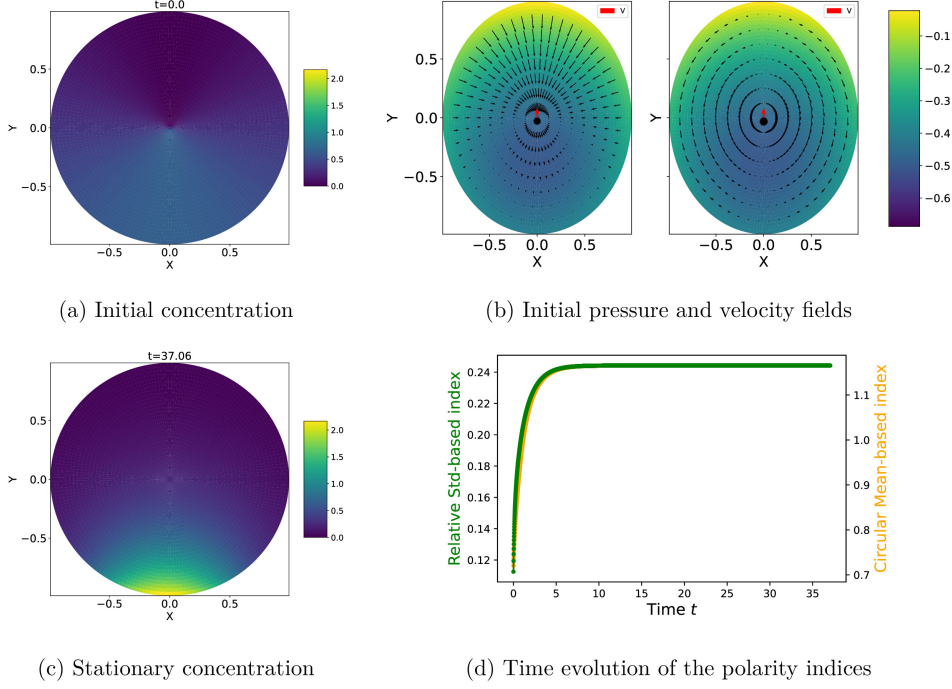


Fig. 4 Illustration of the convergence of the system towards a travelling stationary state, with $D = 0.3$, $\chi = 1 < \chi_0 = 1.2$, $c_t = 1$ and $\gamma = 0.5$. (a): Polarised initial concentration given by Equation (46). (b): Initial pressure field given by Lemma 6, together with the corresponding radial (left) and angular (right) advection fields and the global cell velocity (red). (c): Stationary non radially-symmetric molecular concentration. (d): Time evolution of the polarity indices (RSD in green, RVL in yellow)

4.4 Parameter spaces

This Subsection is devoted to showing parameter spaces for both the Relative Standard Deviation and the Resultant Vector Length at stationary state, depending on the parameters χ and either D or ct . The initial concentration is given by Equation (46),

and the threshold for numerical stationary state is taken equal to 10^{-6} . The results are given in Figure 5. Subfigures (a)–(b) treat the pair (c_t, χ) and show both unpolarised and polarised stationary states. One can see that below a threshold value on χ the concentration converges towards the radially-symmetric profile, and that this threshold increases slowly with c_t . Subfigures (c)–(d) treat the pair (D, χ) , and also present both unpolarised and polarised stationary states. It is observed that both polarity indices decrease as the diffusion coefficient increases, as expected. Moreover, an affine relation between both parameters seems to rule the transition between both types of stationary states. Corollary 13 stated the existence of travelling stationary solutions for $\chi < \chi_0 = 4D$. One can see that it is also the case for $\chi \geq 4D$. All in all, these parameter spaces illustrate numerically the transition from unpolarised to polarised stationary states depending on the parameters.

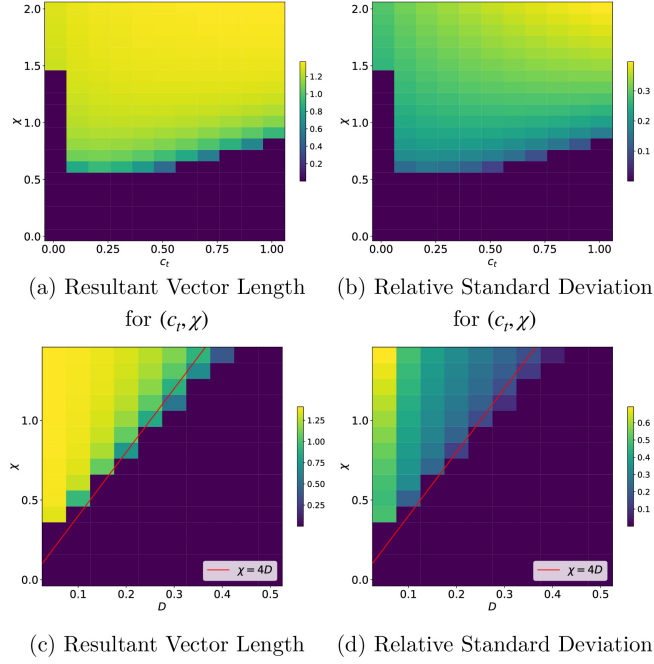


Fig. 5 Parameter spaces of polarity indices at stationary state as a function of the boundary pressure amplitude χ and either the half-saturation threshold c_t (top) or the molecular diffusion coefficient D (bottom). The initial condition is given by Equation (46). (a-c): Resultant Vector Length. (b-d): Relative Standard Deviation. The relation $\chi = 4D$ is shown in red in the (D, χ) parameter spaces. Parameters: $(\gamma, D, c_t) = (0.1, 0.3, 0.4)$; threshold for numerical stationary state: 10^{-6} ; $(\Delta t, N_\theta) = (0.01, 120)$, $\Delta r = \Delta\theta = \frac{2\pi}{N_\theta} \simeq 0.05$

5 Discussion

Modelling

The construction of the deterministic model is based on several assumptions. Firstly, selecting a solid disc as cell domain is a limitation, chosen to focus on the interplay between the actin cytoskeleton and a molecular species in intracellular dynamics. Secondly, the main novelty of our approach is the description of the actin cytoskeleton as an active fluid. The constitutive equations are based on the following elements: actin polymerisation at the boundary inhibited by the molecular species, depolymerisation within the domain, and friction forces resulting from actin flow from the boundary towards the centre. The reduction of the problem to the Darcy-Poisson problem (2)–(3) follows from neglecting fluid viscosity compared to friction forces, which is relevant for a crawling cell, and assuming that the pressure instantaneously enforces a constant actin density, as in previous studies [23]. The assumption of constant actin density is a simplification consistent with the use of a solid domain: the actin activity translates directly into pressure, as no deformation is possible. The model can be further compared with [4]. Indeed, in the cited work the mean space-averaged actin velocity u^* in 1D is given by

$$u^*(t) = -\beta \left(\frac{c(t, 0)^n}{C_s^n + c(t, 0)^n} - \frac{c(t, L)^n}{C_s^n + c(t, L)^n} \right), \quad (48)$$

where $n \in \mathbb{N}$ and $C_s > 0$. This was formally justified from active gel models of cytoskeleton as found in [7], leading to a second-order ODE on the actin velocity with Dirichlet boundary conditions such as $u(t, 0) = u_0 - \alpha \frac{c(t, 0)^n}{C_s^n + c(t, 0)^n}$, $\alpha > 0$. In our model, we used a similar feedback directly on the actin density, yielding a Dirichlet boundary condition in a second-order Poisson problem on the pressure. Then, computing the space-averaged actin velocity given by Equations (2)–(4) for k_p given by Equation (5) yields

$$\int_{\Omega} u(t, \mathbf{x}) \, d\mathbf{x} = \chi(\gamma\pi - 1) \int_{\partial\Omega} \frac{c(t, \mathbf{x})}{c_t + c(t, \mathbf{x})} \mathbf{n} \, d\sigma(\mathbf{x}),$$

recovering a similar expression, where, up to spatial normalisation, the coupling parameter β from Equation (48) corresponds to $\chi(\gamma\pi + 1)$. Moreover, in [4], the cell velocity is proportional to the actin velocity, with $v = -u^*$. Our framework allows to go beyond this simplifying assumption, since one can write

$$\int_{\Omega} u(t, \mathbf{x}) \, d\mathbf{x} = -\pi v(t) - \chi \int_{\partial\Omega} \frac{c(t, \mathbf{x})}{c_t + c(t, \mathbf{x})} \mathbf{n} \, d\sigma(\mathbf{x}).$$

This highlights how the model now captures the dissociation between the internal activity and the external motion. Indeed, on a nonadhesive substrate, a polarised cell could generate sustained actin flows while not moving, since no friction forces convert the internal activity into driving forces. This amounts to taking $\gamma = 0$: the cell velocity is null, while a net global actin velocity may still exist. Furthermore, when $\gamma \neq 0$, then

$$|v(t)| = \frac{\gamma}{1 + \pi\gamma} \left| \int_{\Omega} u(t, \mathbf{x}) \, d\mathbf{x} \right| < \left| \int_{\Omega} u(t, \mathbf{x}) \, d\mathbf{x} \right|,$$

in coherence with the expected cell behaviour moving slower than its driving internal flows. To summarise, our 2D modelling approach allows to justify the 1D model from [4]. Furthermore, our model allows to decipher local effects related to actin flows from global effects linked with cell displacement. The model relies on 4 parameters: the molecular diffusion coefficient D , the molecular activation saturation coefficient c_t , the minimal boundary pressure value χ , the velocity coefficient γ .

Mathematical analysis

The present work can be compared with the results obtained for the related one-dimensional model studied in [33], which considered a linear boundary pressure term and an actin velocity depending only on the pressure gradient. In that case, a resting stationary state was identified for a subcritical mass. In the supercritical case, for certain initial conditions, it was shown that blow-up occurred in finite time. From a modelling perspective, this was regarded as a degenerate polarised state. In the present work, under certain parameter conditions, we proved the existence of both resting and travelling stationary states as well as the linear stability of the resting stationary state. We did not observe a numerical blow-up, which may be due to the Hill activation term ensuring boundedness of the pressure boundary terms.

Numerical simulations

Numerical simulations produced both polarised and unpolarised cell regimes, depending on the balance between the strength of molecular inhibition of inward flow and both molecular diffusion and molecular activation.

The numerical simulations also allowed investigation of the mathematical conditions on parameters obtained in Propositions 8, 10 and 12. They suggested that the existence of both stationary states extends beyond the theoretical conditions: in particular, polarised travelling solutions are observed numerically far from the local bifurcation branch identified in Proposition 12, indicating that the proofs may have technical limitations. The model exhibits a complex competition between different processes: the molecular diffusion typically competes with advection, but the advection field itself arises from a trade-off between self-reinforcing molecular asymmetry at the boundary and depolymerisation, which drifts molecules towards the cell centre. In this context, identifying strong conditions for the existence of a given regime is challenging. Numerical simulations also indicate that the threshold on χ for linear stability of the resting stationary state is not optimal.

From a numerical perspective, using a first-order linear upwind scheme prevented spurious oscillations in the solution, but also introduced some numerical diffusion. We found that taking $N_\theta = 200$, hence $\Delta r = \Delta\theta \simeq 0.03$, was sufficient to maintain a manageable computational cost while reducing the error, as seen in Figure 3.

6 Conclusions

This work aims to formulate a two-dimensional model for single-cell migration based on the mechano-chemical coupling between the actin cytoskeleton and a regulatory

molecular species, as presented in [4]. The achieved objective was to provide a fully spatial framework and to justify the phenomenological formulation of the actin velocity considered therein. The actin velocity field is described as an active fluid with constitutive equations based on both actin polymerisation and friction forces arising from actin flows and cell displacements. Consequently, cell polarisation occurs due to the coupling between the fluid and the molecular species, and is associated with persistence of motion. The mathematical analysis of the resulting nonlinear, nonlocal model characterises both resting and travelling stationary regimes, as illustrated by numerical simulations.

Future work should focus on stochastic perturbations of the model to produce numerical cell trajectories, which would then be compared with the active particle model introduced in [4]. Furthermore, we ought to take advantage of both mechanical and chemical descriptions of the intracellular dynamics to investigate the cell interaction with the environment. Indeed, this approach allows each type of interaction to be considered at the appropriate level. The entire intracellular activity then adapts to the external cue. As a result, investigating phenomena such as chemotaxis or guidance by mechanical obstacles will be of interest.

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Ethics approval and consent to participate

Not applicable

Consent for publication

All authors gave their consent for publication

Data availability

Not applicable

Materials availability

Not applicable

Code availability

The Python script used to perform the numerical simulations is available upon request to the corresponding author.

Author contribution

Conceptualization: Nicolas Meunier and Raphaël Voituriez ; Methodology: Nicolas Meunier ; Formal analysis and investigation: Christèle Etchegaray and Nicolas Meunier ; Writing - original draft preparation: Christèle Etchegaray and Nicolas Meunier ; Writing - review and editing: Christèle Etchegaray and Nicolas Meunier ; Supervision: Nicolas Meunier and Raphaël Voituriez

Appendix A Numerical framework and cell polarity indices

In this part, we detail the finite volumes numerical framework used to perform the numerical simulations. Then, we detail and illustrate the cell polarity indices used to characterise the internal cell dynamics.

A.1 Numerical framework

The radial discretization is given by $\{r_j = j \Delta r, j = 1 \dots N_r\}$, where $r_{N_r + \frac{1}{2}} = 1$. Similarly, the angular discretization is given by $\{\theta_k = k \Delta \theta, k \in 1 \dots N_\theta\}$, with $\theta_{N_\theta} = 2\pi$. For $j \in \{1 \dots N_r\}$ and $k \in \{1 \dots N_\theta\}$, the control volumes $W_{(j,k)} \subset \mathbb{R}^2$ are given by

$$W_{(j,k)} = \left(r_{j-\frac{1}{2}}, r_{j+\frac{1}{2}}\right) \times \left(\theta_{k-\frac{1}{2}}, \theta_{k+\frac{1}{2}}\right),$$

such that $|W_{(j,k)}| = r_j \Delta r \Delta \theta$. The central control volume is given by $W_0 = B(0, r_{\frac{1}{2}})$ such that $|W_0| = \pi r_{\frac{1}{2}}^2$. We use a finite volumes scheme in space. More precisely, keeping the same notation for simplicity, the discretised values of the molecular concentration at time $t > 0$ are given by

$$\begin{cases} c_0(t) := \frac{1}{\pi r_{\frac{1}{2}}^2} \iint_{B(0, r_{\frac{1}{2}})} c(t, r, \theta) r \, dr \, d\theta, \\ c_{j,k}(t) := \frac{1}{|W_{(j,k)}|} \iint_{W_{(j,k)}} c(t, r, \theta) r \, dr \, d\theta, \quad j \in \{1 \dots N_r\}, k \in \{1 \dots N_\theta\}, \end{cases}$$

and their time dynamics are obtained using Equation (1). The advection term based on Equations (2)–(4) is approximated using a first-order upwind scheme. Finally, let $\{t^n = n \Delta t, n = 0 \dots N_f\}$ be the time discretization, with $T_f := t^{N_f}$ the final time of the simulation. Then, $(c_{j,k}^n := c_{j,k}(t^n))_{1 \leq j \leq N_r, 1 \leq k \leq N_\theta}$ and $c_0^n := c_0(t^n)$ are the fully discretised values of the solution at time t^n obtained using an Euler scheme. Unless indicated otherwise, we take $\Delta t = 0.01$, and $N_\theta = 200$, so that $\Delta r = \Delta \theta = \frac{2\pi}{N_\theta} \simeq 0.03$.

A.2 Cell polarity indices

Two cell polarity indices are considered in this paper.

- the Relative Standard Deviation (RSD) or Coefficient of Variation (CV) is given by the perimeter-normalized ratio between the standard deviation of $\{c_{N_r,k}^n\}_{1 \leq k \leq N_y}$ and its mean value $\bar{c}^n := \frac{1}{N_\theta} \sum_{k=1}^{N_\theta} c_{N_r,k}^n$. More precisely,

$$\text{RSD}^n := \frac{1}{2\pi\bar{c}^n} \sqrt{\frac{1}{N_y} \sum_{k=1}^{N_y} |c_{N_r,k}^n - \bar{c}^n|^2}.$$

- the normalized Mean Resultant Vector is given by

$$RV^n := \frac{1}{\sum_{i=1}^{N_\theta} c_{N_r,k}^n} \sum_{i=1}^{N_\theta} c_{N_r,k}^n \mathbf{e}_k$$

as defined in circular statistics [37]. Its norm, the Resultant Vector Length (RVL) provides another polarisation index.

Figure A1 shows some boundary concentration profiles together with the corresponding RSD and RVL values. In Subfigure A1–(a), the boundary concentration is constant, both indices are null and the cell is in a resting state. In Subfigure A1–(b), the boundary concentration shows a single pole, both the RSD and the RVL are nonzero, and the cell is in a travelling state. In Subfigure A1–(c), the boundary concentration shows two symmetric poles, such that the cell is in a resting state and the RVL is zero while the RSD is nonzero. Finally, in Subfigure A1–(d), the boundary concentration shows a steep polarisation associated with a travelling state. However, both polarity indices are smaller than in Subfigure A1–(b), although nonzero.

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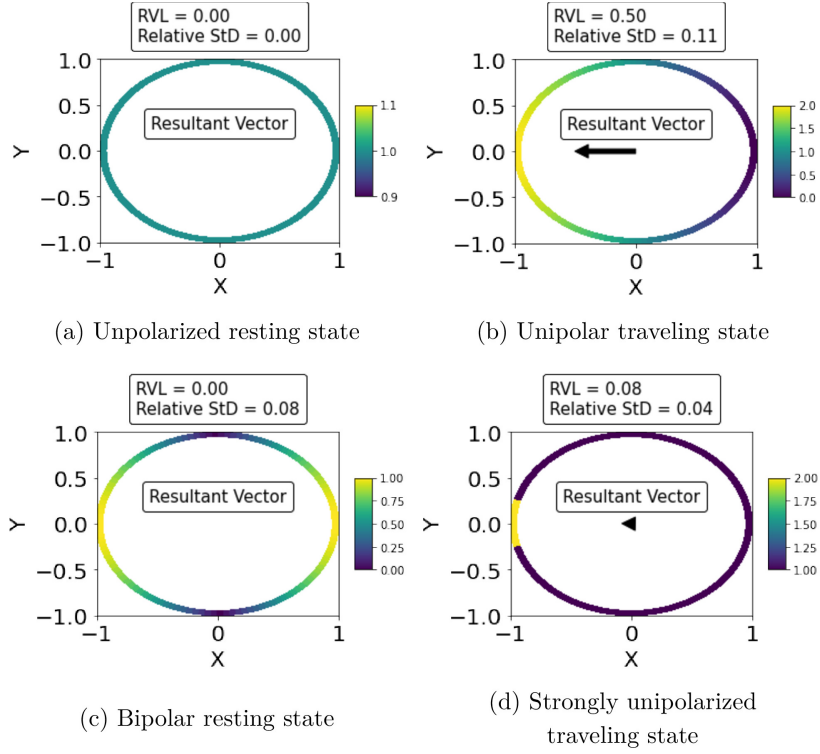


Fig. A1 Several boundary concentration profiles with the corresponding polarity indices. (a): Homogenous boundary concentration associated with a resting state, with null Relative Standard Deviation and Resultant Vector Length. (b): Unipolar boundary concentration given by $\theta \mapsto 1 - \cos(\theta)$, associated with a travelling state, characterised by nonzero Relative Standard Deviation and Resultant Vector Length. (c): Boundary concentration given by $\theta \mapsto \cos(\theta) (\mathbb{1}_{[-\pi/2, \pi/2]} - \mathbb{1}_{[\pi/2, 3\pi/2]})$, showing two opposite poles and associated with a resting state. The Relative Standard Deviation is nonzero while the Resultant Vector Length is zero. (d): Boundary concentration given by $\theta \mapsto 2\mathbb{1}_{[\pi-5\Delta\theta, \pi+5\Delta\theta]}$, with a steep polarisation associated with a travelling state. Both Relative Standard Deviation and Resultant Vector Length are nonzero, although smaller than case (b).

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