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A nonlinear system to model communication between yeast cells during their mating process

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Abstract

In this work, we develop a model to describe some aspects of communication between yeast cells. It consists in a coupled system of two one-dimensional nonlinear advection-diffusion equations in which the advective field is given by the Hilbert transform. We give some sufficient condition for the blow-up in finite time of the coupled system (formation of a singularity). We provide a biological interpretation of these mathematical results.

1 Introduction

In this work, we address an old and universal problem in cell biology: how do cells communicate with each other? We consider here the communication between two yeast cells during their mating. We propose and study a model in which the dynamics of the polarization markers of each cell depends on the organization of its cytoskeleton and the amount of pheromone released by the mating partner. If the two cells polarize opposite each other then we consider that they are communicating.

More precisely, we model the two cell membranes as two parallel lines separated by a distance h from each other (see Figure 1). The state of each cell is characterized

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by the distribution on its membrane of a protein involved in the process of polarization, Cdc42 e.g., with density $\nu_i(t, x)$, where t is the time and x is a position on the membrane (abstractly described as a real line). The more $\nu_i(t, x)$ is concentrated around a point, say x_0 , the more polarized the cell is at that point x_0 . The extreme polarized situation is one with $\nu_i(t, x) dx = C\delta_{x_0}$, where δ_{x_0} is the Dirac mass.

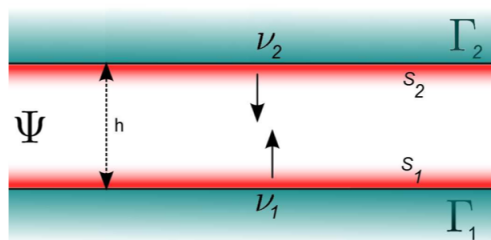


Figure 1: Tangential model for the communication between two cells

The model consists of the following system, for $(t, x) \in \mathbb{R}_+ \times \mathbb{R}$:

$$(1) \quad \begin{cases} \partial_t \nu_1(t, x) &= \partial_{xx} \nu_1(t, x) + \chi \partial_x (\nu_1 \mathcal{H}(S_2 \nu_1))(t, x), \\ \partial_t \nu_2(t, x) &= \partial_{xx} \nu_2(t, x) + \chi \partial_x (\nu_2 \mathcal{H}(S_1 \nu_2))(t, x), \end{cases}$$

with initial data $\nu_1(0, x) = \nu_{1,0}(x)$ and $\nu_2(0, x) = \nu_{2,0}(x)$.

Here \mathcal{H} is the Hilbert transform, $\chi > 0$ is a given parameter and $S_i = S_i(t, x)$, $(t, x) \in \mathbb{R}_+ \times \mathbb{R}$ are functions, describing the density of the pheromone produced by the cell $\#i$, given by the expression

$$(2) \quad S_i(t, x) = F_h * \nu_i(t, x),$$

with F_h defined by

$$(3) \quad F_h(x) = F\left(\sqrt{x^2 + h^2}\right).$$

Thereby, h is a parameter characterizing the distance between the cells.

We assume that F satisfies the following assumptions:

(A1) F is smooth, $\mathcal{C}^\infty(\mathbb{R}_+)$ and nonnegative,

(A2) F is decreasing to 0.

(A3) F is globally Lipschitz, so that in particular $\sup_{[h, +\infty[} |F'| < +\infty$ and

$$|F'_h(x)| = \left| \frac{x}{\sqrt{x^2 + h^2}} F'(\sqrt{x^2 + h^2}) \right| \leq \sup_{[h, +\infty[} |F'|.$$

Briefly, the main assumptions that lead to (1) are as follows. On each cell membrane, proteins can either diffuse freely or be actively transported (via the actin

filaments forming the cytoskeleton) to regions of high protein and external signal (pheromone produced by the opposite cell type) concentrations. Proteins located on the membrane have two effects on cells by amplifying active transport in both cells through the production of signals. The underlying processes are: nucleation of actin filaments in one cell and secretion of external signalling molecule (pheromone) which can bind to the other cell. We refer to Section 2 for a detailed presentation of the model with biological motivations.

Note that the total molecular contents are conserved for each cell in (1). For the sake of simplicity, throughout this work we will apply the scaling $\nu_i \rightarrow \nu_i/M_i$, $\chi \rightarrow M_1 M_2 \chi$ which turns out to be equivalent to assuming that both cells have the same total molecular content on their membrane:

$$(4) \quad M_1 = \int_{\mathbb{R}} \nu_1(t, x) dx = M_2 = \int_{\mathbb{R}} \nu_2(t, x) dx = 1.$$

Hence, the model is characterised by the parameter χ and the definitions of S_i .

The mathematical question which arises in this class of models is to determine which contribution will dominate, either aggregation by directed chemoattraction or dispersion by stochastic diffusion. Before stating our results about the analysis of (1) – (2), let us briefly comment the literature. The uncoupled problem, corresponding to a single cell ($\#i = 1$) in a constant field of pheromon concentration ($S_2 \equiv 1$) is a one-dimensional version of a class of active transport models introduced in [5] and validated in [18] for the modelling of yeast cell polarization. This uncoupled problem is similar to the Modified Keller-Segel (MKS) introduced and studied in [7], where it was proved that above a critical mass some singularity occurs (so called blow-up). This dichotomy between concentration of the solution vs. self-similar decay is analogous to the classical Keller-Segel equation for chemotaxis [2]. The aforementioned works deal with only one density (of proteins or attracting cells).

In the present work, we show that some results can be extended to the nonlinear coupling between two PDEs, with some similarities, same type of reasoning to derive the critical mass, but also important differences since we show that the critical mass is a necessary but not sufficient condition to trigger the blow-up.

First, we consider the situation where both cells are dynamic and we find a condition for which global existence of solutions of the system (1) – (2) is not possible, that is a singularity or blow-up occurs in finite time. To do so we compute informally the time derivative of the joint second moment $\mathcal{E}(t)$ defined by

$$(5) \quad \mathcal{E}(t) := \iint_{\mathbb{R}^2} \frac{(x - y)^2}{4} \nu_1(t, x) \nu_2(t, y) dx dy > 0.$$

Our aim is to study the dynamics and the sign of \mathcal{E} . If \mathcal{E} cannot remain positive for all time, there is an obstruction to global existence. Such a technique was first used by Nagai [19], then by many authors in various contexts (see [23] and references therein).

Our first result is an obstruction to global existence and we consider a particular situation in which the blow up can be established for the system (1) – (2).

Define χ^* by

$$(6) \quad \frac{\chi^* F(h)}{2\pi} = 1.$$

Proposition 1.1 (Critical threshold). *Assume that F satisfies (A1) – (A2), $\chi > \chi^*$ and $\mathcal{E}_0 = \mathcal{E}(t=0)$ is small enough so that*

$$(7) \quad \sqrt{\mathcal{E}(0)} < \frac{\pi}{2\chi \sup_{[h, +\infty[} |F'|} \left(\frac{\chi F(h)}{2\pi} - 1 \right).$$

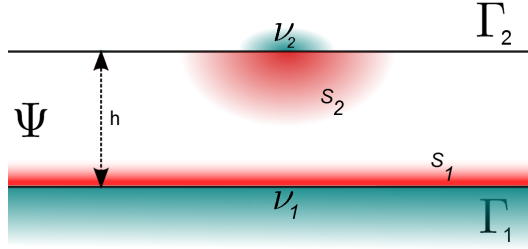
There is an obstruction to global existence of the solution (ν_1, ν_2) of (1) – (2) since $\mathcal{E}(t)$ would vanish in finite time.

Remark 1. *In the unscaled variables, the critical mass (6) is given by*

$$M_1 M_2 > \frac{2\pi}{\chi F(h)}.$$

In a second step, to better understand the dynamics of the system (1) – (2) we study the extreme situation where cell #2 is already polarized, i.e. $\nu_2 dx = \delta_{x=0}$ and we investigate how it affects cell #1, see Fig. 2. We find that there exists a threshold distance under which cell #1 does not "feel" her potential polarized partner cell #2.

Figure 2: Representation of a polarized cell in front of an active cell



As before, we assume that ν_1 is solution of

$$(8) \quad \partial_t \nu_1(t, x) = \partial_{xx} \nu_1(t, x) + \chi \partial_x (\nu_1(t, x) \mathcal{H}(S_2 \nu_1)(t, x)), \quad (t, x) \in \mathbb{R}_+ \times \mathbb{R},$$

with $S_2 = F_h * \delta_{x=0}$ corresponds to the formula given by (2). We define the second moment by

$$(9) \quad I_2(\nu_1)(t) = \frac{1}{2} \int_{\mathbb{R}} x^2 \nu_1(t, x) dx.$$

Proposition 1.2. *Assume that F satisfies (A1) – (A2), and that $\int_{\mathbb{R}} (\nu_1^0)^2 + I_2(\nu_1^0) < +\infty$, then there exists a solution ν_1 to (8) on associated time interval $[0, T)$. Moreover, the second momentum $I_2(\nu_1)(t)$ has the following behaviour*

- If $\chi < \chi^*$, then $I_2(\nu_1)(t)$ is positive for all existence time $t \in [0, T)$,

- if $\chi > \chi^*$ (being defined by (6)) and $F\left(\sqrt{I_2(\nu_1)(0) + h^2}\right) > \frac{1}{2} + \frac{\pi}{\chi}$, then $I_2(\nu_1)$ becomes negative in finite time. In such a case one has $T < +\infty$.

Finally, we describe here a few computations showing that, although not optimal, condition (7) is not a technical artifact. We show how supercritical data might end up with global existence because dialog is not triggered.

Proposition 1.3. *Consider $(\nu_{1,0}, \nu_{2,0}) \in (L^1(\mathbb{R}))^2 \cap (L^2(\mathbb{R}))^2$, nonnegative such that $\|\nu_{1,0}\|_1 = \|\nu_{2,0}\|_1 = 1$. There exists $\eta > 0$, depending on the parameters of the system, such that if*

$$\iint_{\mathbb{R}^2} \frac{\nu_{1,0}(x)\nu_{2,0}(y)}{1 + (x - y)^2} dx dy \leq \eta,$$

then the solution of (1) – (2) exists globally. Moreover, the L^2 norms $\|\nu_i\|_2$ are decreasing towards 0 in long time.

Remark 2. *Interestingly, we can choose an "absolute" parameter η that does not depend on the values of $\|\nu_i\|_2$. We can apply this result even to initially very concentrated data.*

The space L^2 is not necessarily optimal for existence considerations ($L \log L$ might be more accurate), but we just want to emphasize the fact that a possible blow up is not instantaneous (i.e. the existence time T satisfies $T > 0$).

The article is organized as follows. First in Section 2, we justify the model from a biological point of view and we discuss our results. In section 3 we prove Proposition 1.1 (the critical χ part), local existence consideration is postponed to section 5. In section 4 we prove Proposition 1.2. In section 5 we perform log and L^2 type estimates for (8) and L^2 estimates for (1) – (2). In Section 6 we prove proposition 1.3.

2 Model construction and discussion of the main results

In this section we first give the biological justification of the equation (8), in the context of yeast cell polarization, which is the focus of the present work.

Next, we discuss the relationship between this model and the so-called modified Keller-Segel (MKS) model: [4, 7]. The latter is based on properties of the Hilbert transform. We also recall some mathematical properties of the MKS model.

2.1 A validated model for the polarization of yeast cells, [18]

Cell polarization describes the process by which a cell transitions from a spherically symmetric shape to a state with a preferred axis. The molecular pathways involved in cell polarization have been studied experimentally in some detail over the past decade, and the results suggest that several alternative mechanisms may be at work, see [25] for a discussion of the different possible feedback loops from a biological viewpoint. Several mathematical models have been proposed in the past decade, see [21, 10] for a review. They incorporate many aspects of the molecular

mechanisms involved in pheromone-induced protein aggregation. They are mainly reaction-diffusion equations. A first class of model describes a mechanism which is based on so-called history and assumes that each division event leaves a localized scar with specific molecular markers (Bud1 proteins) that are attached to the cell membrane and can initiate subsequent polarization events [15, 25, 26, 8, 28, 29]. In these models, the symmetry of the actin filaments is broken from the start. The authors seek to describe how the spatial dynamics of Cdc42 is linked to that of actin cables. A second mechanism proposed in the literature is based on Turing instability and involves the Bem1 protein, see [20, 11, 12, 22, 9, 16]. This presumably combines small diffusion of some activator on the membrane, and large diffusion of some inhibitor in the cytoplasm. We also quote [17] which proposes a segregation model which does not rely on the Turing instability, but on substrate limitation.

In this work, following [6, 5, 18], we focus on a third mechanism that is based on the active transport of polarity markers along cytoskeleton filaments. The cellular cytoskeleton is a network of long semi-flexible filaments made of protein subunits [24]. These filaments (mainly actin or microtubules) act as roads along which motor proteins are able to perform biased ballistic movement and transport various molecules, in a process that consumes the chemical energy of adenosine triphosphate (ATP).

In the case of yeast polarization, it has been proposed that this actin-based mechanism relies on a positive feedback loop in the dynamics of polarity markers, which is mediated by the actin cytoskeleton [28]. It has been shown that polarity markers (Cdc42 proteins) activate actin filament polymerization when adsorbed on the cell membrane, so that active transport along filaments pointing to Cdc42-enriched regions is promoted in the cell cytoplasm. The positive feedback loop then results from the fact that the Cdc42 markers themselves are actively transported into the cytoplasm, and are thus preferentially directed to the high concentration regions. Other factors, such as the Bem1-mediated positive feedback e.g., are not present in the model considered here. Indeed, we believe it is of interest to investigate the potentiality of a mass-preserving mechanism to account for symmetry breaking in the cell content.

Suppose that the cell is represented by the half-space $\mathbf{H} = \mathbb{R} \times (0, +\infty)$ and that the spatial variable is $\mathbf{x} = (x, z)$. We denote by $n(t, \mathbf{x})$ the concentration in the cytoplasm of proteins (or markers) involved in cell polarization (Cdc 42 for example), by $\mu(t, x)$ the concentration of proteins trapped at the boundary and by $c(t, \mathbf{x})$ the density of actin filaments in the cytoplasm of the cell. The model first introduced in [5] and validated in [18] is :

$$(10) \quad \partial_t n(t, \mathbf{x}) = \Delta n(t, \mathbf{x}) - \chi \nabla \cdot (n(t, \mathbf{x}) \nabla c(t, \mathbf{x})), \quad t > 0, \quad \mathbf{x} \in \mathbf{H},$$

completed by the flux boundary condition:

$$(11) \quad \partial_z n(t, x, 0) - \chi n(t, x, 0) \partial_z c(t, x, 0) = -\partial_t \mu(t, x), \quad x \in \mathbb{R}.$$

Furthermore, the dynamic exchange of markers at the boundary occurs with an attachment rate k_{on} and a detachment rate k_{off} , hence the time evolution of $\mu(t, x)$

is

$$(12) \quad \partial_t \mu(t, x) = k_{\text{on}} n(t, x, 0) - k_{\text{off}} \mu(t, x).$$

We have formally conservation of the molecular content:

$$(13) \quad M = \int_{\mathbf{H}} n_0(\mathbf{x}) d\mathbf{x} + \int_{\mathbb{R}} \mu_0(x) dx = \int_{\mathbf{H}} n(t, \mathbf{x}) d\mathbf{x} + \int_{\mathbb{R}} \mu(t, x) dx, \quad \forall t \geq 0.$$

In this model advection, that is $\chi \nabla c$, describes the active transport of proteins along actin filaments. The nucleation of new filaments is assumed to occur at the cell boundary, under the combined action of molecules trapped on the boundary and external pheromone molecules. After a dimensional analysis, the model that describes the density of actin filaments is the following

$$(14) \quad \begin{cases} -\Delta c(t, \mathbf{x}) = 0, & \mathbf{x} \in \mathbf{H}, \\ \partial_z c(t, x, 0) = -S(t, x)\mu(t, x), & x \in \mathbb{R}. \end{cases}$$

2.2 Heuristic justification of (1)

Let us start by recalling some properties of the Hilbert transform. Then we will see the heuristic connection between the models (8) and (10) – (14).

The Hilbert transform of a function $f \in L^p(\mathbb{R})$, $1 \leq p < \infty$ is defined as the Cauchy principle value integral [27]

$$(15) \quad \mathcal{H}(f)(x) = \frac{1}{\pi} p.v. \int_{\mathbb{R}} \frac{f(y)}{x - y} dy.$$

The use of the Hilbert transform in our model is justified by the following lemma (for which we give the main formal arguments).

The Hilbert transform maps L^p to itself for any $1 < p < +\infty$,

$$(16) \quad \|\mathcal{H}(f)\|_p \leq C_p \|f\|_p,$$

with $C_2 = 1$.

Obviously, the integral (15) exists for almost all x .

Lemma 2.1. *The solution of (14) is*

$$(17) \quad c(t, x, z) = -\frac{1}{\pi} \int_{x' \in \mathbb{R}} \log \left(\sqrt{(x - x')^2 + z^2} \right) S(t, x') \mu(t, x') dx',$$

and it holds that

$$\partial_x c(t, x, 0) = -\mathcal{H}(S\mu)(t, x).$$

Proof. The fact that the log kernel formulation leads to $-\Delta c = 0$ is classical and we do not repeat the computations. We simply check the normal boundary condition. Define the function P by

$$P(x) = \frac{1}{\pi} \frac{1}{x^2 + 1} \quad \forall x \in \mathbb{R}.$$

Let $\varepsilon > 0$, define the Poisson kernel by

$$(18) \quad P_\varepsilon(x) = \frac{1}{\varepsilon} P\left(\frac{x}{\varepsilon}\right).$$

Since

$$\|P\|_{L^1(\mathbb{R})} = \|P_\varepsilon\|_{L^1(\mathbb{R})} = \pi,$$

the family $(P_\varepsilon)_\varepsilon$ is an approximation of the unity. The conjugate Q_y is defined by

$$(19) \quad \forall(x, y) \in \mathbb{R} \times \mathbb{R}_+, \quad Q_y(x) = \frac{1}{y} Q\left(\frac{x}{y}\right),$$

with

$$Q(x) = \frac{1}{\pi} \frac{x}{x^2 + 1} \quad \forall x \in \mathbb{R}.$$

A straightforward computation leads to for $x > 0$

$$\begin{aligned} \partial_z c(t, x, z) &= -\frac{1}{\pi} \int_{\mathbb{R}} \frac{z}{(x-x')^2 + z^2} S(t, x') \mu(t, x') dx' \\ &= -\frac{1}{\pi} \int_{\mathbb{R}} \frac{z}{y^2 + z^2} S(t, x+y) \mu(t, x+y) dy \\ &= -P_z * (S\mu)(t, x) \\ &\rightarrow -S(t, x) \mu(t, x), \quad z \rightarrow 0. \end{aligned}$$

We then verify the second point (formally)

$$\begin{aligned} \partial_x c(t, x, z) &= -\frac{1}{\pi} \int_{\mathbb{R}} \frac{x-x'}{(x-x')^2 + z^2} S(t, x') \mu(t, x') dx' \\ &= -Q_z * (S\mu)(t, x) \\ &\rightarrow -\mathcal{H}(S\mu)(t, x), \quad z \rightarrow 0. \end{aligned}$$

The proof of the convergence can be found (with more details) in [27], for instance. \square

We finally note that all calculations involving the Hilbert transform can be done by first imposing that $|x - x'| \geq \varepsilon$ and $|y - y'| \geq \varepsilon$ and then letting ε go to 0. Therefore, for the sake of brevity throughout this work, we will omit writing the principal value in the definition of the Hilbert transform, (15).

2.2.1 Heuristics leading to (10) – (14)

In the supercritical case, i.e., when M is large, numerical simulations, see [5, 3], suggest that the solution $n(t, \mathbf{x})$ of (10) – (14) concentrates on the boundary $\{y = 0\}$. Assuming that $n(t, x, y) = \nu(t, x) \delta(y = 0)$, we can formally write the dynamics of $\nu(t, x)$ as follows:

$$\partial_t \nu(t, x) = \partial_{xx} \nu(t, x) + \chi \partial_x (\nu \mathcal{H}(S\mu))(t, x).$$

Assuming rapid rates, we are approaching a quasi-stationary equilibrium of the two populations, i.e $\mu(t, x) = \frac{k_{\text{on}}}{k_{\text{off}}} \nu(t, x)$ for $x \in \mathbb{R}$, it reads as

$$\partial_t \nu(t, x) = \partial_{xx} \nu(t, x) + \chi S \frac{k_{\text{on}}}{k_{\text{off}}} \partial_x (\nu \mathcal{H}(S\nu))(t, x).$$

2.3 Link between (8) and the MKS system

In this paragraph we detail the links between (8) and the following model, called the modified Keller-Segel system (MKS), and which is written as

$$(20) \quad \begin{cases} \partial_t n(t, x) = \partial_{xx} n(t, x) - \chi \partial_x (n(t, x) \partial_x c(t, x)) & t > 0, x \in \mathbb{R}, \\ c(t, x) = K * n(t, x) & t > 0, x \in \mathbb{R}, \\ n(t = 0, x) = n^0(x) & x \in \mathbb{R}, \end{cases}$$

where $*$ is the usual convolution product and

$$K(z) = -\frac{1}{\pi} \log |z|.$$

Lemma 2.2. *If $c = K * n$, then one has $\partial_x c = -\mathcal{H}(n)$.*

Proof. For all $\varepsilon > 0$, introduce c_ε by

$$\forall x \in \mathbb{R}, \quad c_\varepsilon(x) = \int_{|x-y|>\varepsilon} K(y) c(x-y) dy.$$

We see that $\lim_{\varepsilon \rightarrow 0} c_\varepsilon(x) = c(x)$. Moreover we can compute its spatial derivative

$$\forall x \in \mathbb{R}, \quad \partial_x c_\varepsilon(x) = \int_{|x-y|>\varepsilon} \frac{c(x-y)}{y} dy,$$

from which we deduce

$$\forall x \in \mathbb{R}, \quad \lim_{\varepsilon \rightarrow 0} \partial_x c_\varepsilon(x) = -\frac{1}{\pi} \left(p.v. \frac{1}{x} * c \right) (x) = -\mathcal{H}(c)(x) = \partial_x c(x).$$

□

2.4 Boundary model (1) – (2) for cell-cell communication

In nature, the budding yeast, *Saccharomyces cerevisiae*, exists in either the diploid or haploid state with two possible types (\mathbf{a} or α). Cells of both types secrete a certain pheromone ($S_{\mathbf{a}}$ or S_{α}), Fig. 3, and carry a pheromone receptor to detect the pheromone produced by cells of the opposite type, [13]. In the present work, we propose a model where the release of extracellular pheromone ($S_{\mathbf{a}}$ or S_{α}) depends on the concentration of Cdc42 protein at the membrane. Furthermore, in accordance with the biological literature, [14, 1, 25, 26], we assume that the pheromone

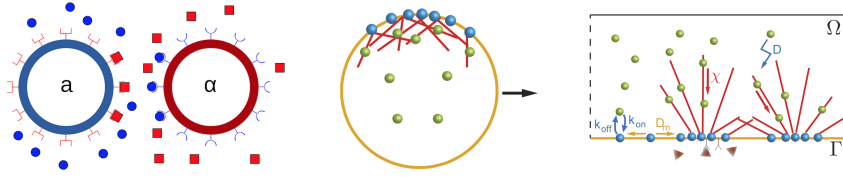


Figure 3: Model for yeast cell communication. On the left, yeast cells of both types secrete some pheromone (\mathbf{a} or α) and bear a pheromone receptor to detect the pheromone produced by the cells of the opposite type. On the middle and on the right a two-dimensional model of protein dynamics inside each cell. The middle panel shows a cell, the right a more detailed view. Actin is polymerized into short filaments, that interact with each other and these are bundled together to form actin cables (which form the cytoskeleton) that cross the cell. The nucleation of filaments is proportional to both the local density of Cdc42 (the proteins that are transported by the cell cytoskeleton in each cell) and to the concentration of pheromone.

contributes to the nucleation of new filaments at the membrane of the opposite type cell, see Fig 3.

This additional level of pairwise cell communication leads to the following rectification of the model (8): for the $\#i$ cell, we consider the advection field to be $\chi\mathcal{H}(S_j\nu_i)$ where S_j is the concentration of pheromone produced by the cell of the opposite type $\#j$. Furthermore, to describe the biological observations, we assume that S_j is produced by ν_j , which means that the pheromone produced by the j -type cell is influenced by the activation level of the opposite cell. Finally, we incorporate a damping factor depending on the intercellular distance. The model consists of the following equations:

$$(21) \quad \partial_t \nu_i(t, x) = \partial_{xx} \nu_i(t, x) + \chi \partial_x \left(\nu_i(t, x) \mathcal{H}(S_j(t, x, h) \nu_i(t, x)) \right),$$

for $(t, x) \in \mathbb{R}_+ \times \mathbb{R}$, $i, j \in \{1, 2\}$ and $j \neq i$, with S_j satisfying the elliptic equation

$$(22) \quad \begin{cases} -\Delta S_j + \lambda S_j = 0, & \text{on } \Psi, \\ \nabla S_j \cdot \mathbf{e}_j = \nu_j, & \text{on } \Gamma_j, \end{cases}$$

where $\mathbf{e}_1 = -\mathbf{e}_2$ denotes the unit outward normal vector to Γ_j .

Let B the Bessel potential

$$(23) \quad B(r) = \frac{1}{4\pi} \int_0^\infty \frac{e^{-\lambda z - \frac{r^2}{4z}}}{z} dz.$$

Note that B satisfies (A1) – (A2), is a convex function and that $x \mapsto F(\sqrt{x})$ is also a convex function. Moreover

Lemma 2.3. *The solution of (22) can be explicitly computed: for all $t > 0$ and $x \in \mathbb{R}$, one has*

$$(24) \quad S_j(t, x, h) = \int_{\mathbb{R}} B(\sqrt{(x-x')^2 + h^2}) \nu_j(t, x') dx'.$$

Proof. Let us introduce the auxiliary function H defined by

$$H(x, y) = \int_0^\infty \int_{\mathbb{R}} \frac{e^{-t - \frac{y^2 + (x-x')^2}{4t}}}{t} \nu_j(x') dx' dt,$$

then,

$$\frac{\partial}{\partial y} H|_{y=0} = \lim_{y \rightarrow 0} - \int_0^\infty \int_{\mathbb{R}} \frac{y}{2t^2} e^{-t - \frac{y^2 + (x-x')^2}{4t}} \nu_j(x') dx' dt.$$

Define the function:

$$I(y) = - \int_0^\infty \int_{\mathbb{R}} \frac{y}{2t^2} e^{-t - \frac{y^2 + (x-x')^2}{4t}} dx' dt,$$

which rewrites as

$$\begin{aligned} I(y) &= - \int_0^\infty \frac{y}{2t^{3/2}} e^{-t - \frac{y^2}{4t}} \int_{\mathbb{R}} \frac{e^{-\frac{(x-x')^2}{4t}}}{\sqrt{t}} dx' dt \\ &= -2\sqrt{\pi} \int_0^\infty e^{-\frac{y^2}{u^2} - \frac{u^2}{4}} du \\ &\xrightarrow{y \rightarrow 0} 4\pi, \end{aligned}$$

where we have performed the change of variable $u = y/\sqrt{t}$ for $y > 0$. Consequently we get

$$\begin{aligned} \frac{\partial}{\partial y} H|_{y=0} - 4\pi\nu_j(x) &= \lim_{y \rightarrow 0} - \int_0^\infty \int_{\mathbb{R}} \frac{y}{2t^2} e^{-t - \frac{y^2 + (x-x')^2}{4t}} (\nu_j(x') - \nu_j(x)) dx' dt \\ &= \lim_{y \rightarrow 0} - \int_0^\infty \int_{\mathbb{R}} \frac{y}{2t^{3/2}} e^{-t - \frac{y^2 + z^2}{4t}} (\nu_j(x+z) - \nu_j(x)) \frac{dz}{\sqrt{t}} dt \\ &= \lim_{y \rightarrow 0} - \int_0^\infty \int_{\mathbb{R}} \frac{y}{2t^{3/2}} e^{-t - \frac{y^2}{4t} - z^2} (\nu_j(x + \sqrt{t}z) - \nu_j(x)) dz dt \\ &= \lim_{y \rightarrow 0} - \int_0^\infty \int_{\mathbb{R}} e^{-\frac{u^2}{y^2} - \frac{u^2}{4} - z^2} \left(\nu_j\left(x + \frac{yz}{u}\right) - \nu_j(x) \right) dz du \\ &= 0. \end{aligned}$$

□

2.5 Discussion of the main results

The present work considers a coupled system of nonlinear convection diffusion equations to describe some aspects of cell-cell communication for yeast cells. For each

cell, the model is one-dimensional, placed on the membrane. As it involves a non-local operator, namely the Hilbert transform, it is sufficiently rich to describe the intracellular interactions between proteins, pheromone and cytoskeleton. The communication between the two cells is induced by the mating pheromone released by the mating partner. This relatively simple system provides both a minimal and quite rich description of the communication between two homologous cells. Its greatest strength lies in its non-linear and non-local character as well as being a system of two coupled equations. Indeed, compared to other models that exist in the literature, this model describes several aspects, namely diffusion, long-range spatial coupling, and receptor endocytosis, which have all been shown to contribute to the establishment and dynamic maintenance of polarized membrane proteins during shmoo formation. Furthermore, this first modeling of the dialogue between cells is new to our knowledge and is based on a polarization model which has been validated with biological data [18]. This model of communication between cells having a very rich behavior, in a next step, we will seek to compare it with biological data.

Our main result is to provide certain conditions (cell-cell distance and protein distribution) for the solution to the system to blow-up. Such a mathematical result is interpreted as an initiation of the dialogue between the two cells.

More precisely, in the case where one of the two cells is polarized, we prove that if the second moment of the second cell and the distance h between the two cells are small enough, then a singularity may occur.

This case is the first step towards modeling the communication between two cells. A natural question is whether the polarization of the #2 cell is sufficient to induce the polarization of the #1 cell in a finite time. In our framework, this question can be rephrased as follows: does the polarization of the #2 cell result in the appearance of a singularity for ν_1 ? We provide a first preliminary answer by establishing that the distance h plays a discriminating role on the second moment $I_2(\nu_1)$ of the protein concentration on the #1 cell when the #2 cell is in a stationary polarized state. By establishing some estimates, we give here a second preliminary answer. Our L^2 estimate tends to give a negative answer to the following question: is instantaneous simultaneous blow-up possible for (1) – (2)? Indeed, if $\nu_2 dx = \delta_{x=0}$, then S_2 given by (2) is such that $S_2 \in L^\infty(\mathbb{R}_+; L^\infty(\mathbb{R}))$. The question of local existence of ν_1 , reduces to the study of equation (8) with $S \in L^\infty(\mathbb{R}_+; L^\infty(\mathbb{R}))$ and will follow from the estimates given in proposition 5.1. Consequently, a solution ν_1 of (1) – (2) may exist locally in time when $\nu_1 dx$ is a mass of Dirac $\delta_{x=0}$. In other words, this means that blow-up during "dialogue" with a Dirac mass is not instantaneous.

Concerning the system (1) – (2), our L^2 estimate result emphasizes the fact that supercritical mass does not systematically lead to blow up. There are two situations that could prevent blow up:

- supercritical but very flat initial data,
- supercritical but far away initial data.

To the best of our knowledge, this work constitutes a first modeling of the dialogue between two cells. We leave a more detailed analysis for a future work and in

particular the question of the apparition of blow-up for (1) – (2) as an open question.

3 Proof of Proposition 1.1

We break the proof of Proposition 1.1 into several lemmas. First we give some notations and preliminary computations in Lemmas 3.1 and 3.2.

For smooth functions g, F and probability measures ν_1, ν_2 on \mathbb{R} , we define the operators \mathcal{R}_1 and \mathcal{R}_2 by

$$(25) \quad \mathcal{R}_1(g, F, \nu_1, \nu_2)(t) = \iint_{\mathbb{R}^2} g(x-y) \mathcal{H}(\nu_1 F * \nu_2)(x) \nu_1(x) \nu_2(y) \, dy \, dx,$$

and

$$(26) \quad \mathcal{R}_2(g, F, \nu_1, \nu_2)(t) = \iint_{\mathbb{R}^2} g(x-y) \mathcal{H}(\nu_2 F * \nu_1)(x) \nu_1(x) \nu_2(y) \, dy \, dx.$$

Lemma 3.1 (preliminary computation). *Let g, F be smooth functions and ν_1, ν_2 probability measures on \mathbb{R} . The following rearrangements hold*

$$\begin{aligned} & \mathcal{R}_1(g, F, \nu_1, \nu_2)(t) \\ &= \frac{1}{2\pi} \iiint \iiint_{\mathbb{R}^4} \frac{g(x-y) - g(x'-y)}{x-x'} F(x'-y') \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx \\ &+ \frac{1}{2\pi} \iiint \iiint_{\mathbb{R}^4} g(x'-y) \frac{F(x'-y') - F(x-y')}{x-x'} \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx, \end{aligned}$$

and

$$\begin{aligned} & \mathcal{R}_2(g, F, \nu_1, \nu_2)(t) \\ &= \frac{1}{2\pi} \iiint \iiint_{\mathbb{R}^4} \frac{g(x-y) - g(x-y')}{y-y'} F(y'-x') \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx \\ &+ \frac{1}{2\pi} \iiint \iiint_{\mathbb{R}^4} g(x-y') \frac{F(y'-x') - F(y-x')}{y-y'} \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx. \end{aligned}$$

Proof. We only prove the first one, the second being similar. Developing the integral we get (formally, but this translates without difficulty for the principal value taking the integral on $\{x-x' > \varepsilon\}$ and letting $\varepsilon \rightarrow 0$ since the final result is properly integrable):

$$\begin{aligned} & \mathcal{R}_1(g, F, \nu_1, \nu_2)(t) \\ &= \frac{1}{\pi} \iiint \iiint_{\mathbb{R}^3} g(x-y) \frac{\nu_1(x') F * \nu_2(x')}{x-x'} \nu_1(x) \nu_2(y) \, dx' \, dy \, dx \\ &= \frac{1}{\pi} \iiint \iiint_{\mathbb{R}^4} g(x-y) \frac{F(x'-y')}{x-x'} \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx \\ &= \frac{1}{2\pi} \iiint \iiint_{\mathbb{R}^4} \frac{g(x-y) F(x'-y') - g(x'-y) F(x-y')}{x-x'} \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx. \end{aligned}$$

The result follows by noticing that

$$\begin{aligned} & g(x-y)F(x'-y') - g(x'-y)F(x-y) \\ = & (g(x-y) - g(x'-y))F(x'-y') + g(x'-y)(F(x'-y') - F(x-y)). \end{aligned}$$

□

Let g be a smooth function on \mathbb{R} and ν_1, ν_2 the solutions of (1), define

$$(27) \quad J_g(t) = \iint_{\mathbb{R}^2} g(x-y)\nu_1(t,x)\nu_2(t,y) \, dy \, dx.$$

From now on, and throughout this article, to lighten the notations we will note $\nu_i(x)$ instead of $\nu_i(t,x)$ the solutions of (1).

Lemma 3.2. *It holds that*

$$(28) \quad \frac{d}{dt} J_g(t) = 2J_{g''}(t) - \chi(\mathcal{R}_1(g', F_h, \nu_1, \nu_2)(t) - \mathcal{R}_2(g', F_h, \nu_1, \nu_2)(t)).$$

Proof. This follows from an integration by parts. □

We can now prove Proposition 1.1. Take $g(z) = \frac{z^2}{4}$ in Lemma 3.2 so that $2J_{g''} = 1$ and

$$\frac{d}{dt} \mathcal{E}(t) = 1 - \chi(\mathcal{R}_1(g', F_h, \nu_1, \nu_2)(t) - \mathcal{R}_2(g', F_h, \nu_1, \nu_2)(t)).$$

Moreover, for $g'(z) = \frac{z}{2}$, we have

$$\begin{aligned} & \mathcal{R}_1(g', F_h, \nu_1, \nu_2)(t) - \mathcal{R}_2(g', F_h, \nu_1, \nu_2)(t) \\ = & \frac{1}{4\pi} \iiint \int_{\mathbb{R}^4} \frac{x-x'}{x-x'} F_h(x'-y') \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx \\ + & \frac{1}{4\pi} \iiint \int_{\mathbb{R}^4} (x'-y) \frac{F_h(x'-y') - F_h(x-y')}{x-x'} \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx \\ - & \frac{1}{4\pi} \iiint \int_{\mathbb{R}^4} \frac{y'-y}{y-y'} F_h(y'-x') \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx \\ - & \frac{1}{4\pi} \iiint \int_{\mathbb{R}^4} (x-y') \frac{F_h(y'-x') - F_h(y-x')}{y-y'} \nu_1(x) \nu_2(y) \nu_1(x') \nu_2(y') \, dy' \, dx' \, dy \, dx. \end{aligned}$$

Recalling that

$$\max \left(\left| \frac{F_h(y'-x') - F_h(y-x')}{y-y'} \right|, \left| \frac{F_h(x'-y) - F_h(x-y)}{x-x'} \right| \right) \leq \sup_{[h, +\infty[} |F'|,$$

we deduce that

$$\begin{aligned} -R & \leq -\frac{1}{2\pi} \iint_{\mathbb{R}^2} F_h(x-y)\nu_1(x)\nu_2(y) \, dy \, dx \\ & \quad + \frac{1}{2\pi} \sup_{[h, +\infty[} |F'| \iint_{\mathbb{R}^2} |x-y|\nu_1(x)\nu_2(y) \, dy \, dx, \end{aligned}$$

hence

$$\begin{aligned}
\frac{d}{dt} \mathcal{E}(t) &\leq 1 - \frac{\chi}{2\pi} \iint_{\mathbb{R}^2} F_h(x-y) \nu_1(x) \nu_2(y) \, dy \, dx \\
&\quad + \frac{\chi}{2\pi} \sup_{[h, +\infty[} |F'| \iint_{\mathbb{R}^2} |x-y| \nu_1(x) \nu_2(y) \, dy \, dx \\
&\leq 1 - \frac{\chi}{2\pi} F_h(0) + \frac{\chi}{2\pi} \sup_{[h, +\infty[} |F'| \iint_{\mathbb{R}^2} |x-y| \nu_1(x) \nu_2(y) \, dy \, dx \\
&\leq 1 - \frac{\chi}{2\pi} F_h(0) + \frac{\chi}{2\pi} \sup_{[h, +\infty[} |F'| \sqrt{\iint_{\mathbb{R}^2} |x-y|^2 \nu_1(x) \nu_2(y) \, dy \, dx} \\
&\leq 1 - \frac{\chi}{2\pi} F_h(0) + \frac{2\chi}{2\pi} \sup_{[h, +\infty[} |F'| \sqrt{\mathcal{E}(t)}.
\end{aligned}$$

Therefore, if we have

$$1 - \frac{\chi F_h(0)}{2\pi} < 0 \quad \text{and} \quad \frac{2\chi \sup_{[h, +\infty[} |F'|}{2\pi} \sqrt{\mathcal{E}(0)} < \left(\frac{\chi F_h(0)}{2\pi} - 1 \right),$$

the quantity $\mathcal{E}(t)$ decreases in time and there is an obstruction to existence beyond time

$$T^* = \frac{\mathcal{E}(0)}{\frac{\chi F_h(0)}{2\pi} - 1 - \frac{2\chi \sup_{[h, +\infty[} |F'|}{2\pi} \sqrt{\mathcal{E}(0)}}}.$$

This achieves the proof of Proposition 1.1.

4 Proof of proposition 1.2

We adapt the steps of the computation of the second joint moment to the case of the system (2). We keep the same notations (remember that now $\partial_t \nu_2 = 0$). So, here $J_g(t) = \int_{\mathbb{R}} g(x) \nu_1(x) \, dx$.

Since $\nu_2(t, x) \, dx = \delta_{x=0}$, recalling (2), we see that

$$(29) \quad S_2(x) = F \left(\sqrt{x^2 + h^2} \right).$$

We break the proof into several lemmas. First in Lemma 4.1, we compute the time derivative of the second momentum $I_2(\nu_1)(t)$. In Lemma 4.2, we find upper and lower bounds. The lower bound allows to conclude in the second case.

Lemma 4.1. *Assume that F satisfies (A1) – (A2), ν_1 is solution of (8) on associated time interval $[0, T)$ and $\nu_2(x) \, dx = \delta_{x=0}$. The time derivative of the second momentum $I_2(\nu_1)(t)$, defined by (9), satisfies*

$$(30) \quad \frac{d}{dt} I_2(\nu_1)(t) = 1 - \chi \mathcal{R}_1(X, F_h, \nu_1, \delta_{x=0})(t).$$

Proof. This follows from an integration by parts. □

Lemma 4.2. *Assume that F satisfies (A1) – (A2), ν_1 is smooth nonnegative solution to (8) with associated time interval $[0, T)$ and $\nu_2(x) dx = \delta_{x=0}$. For all $t \in [0, T)$ the following inequalities hold:*

$$\begin{aligned} & 1 - \frac{\chi F_h(0)}{2\pi} - \frac{\sup_{[h, +\infty[} |F'|}{\pi} \sqrt{I_2(\nu_1)(t)} \\ & \leq \frac{d}{dt} I_2(\nu_1)(t) \leq 1 - \frac{\chi F_h(0)}{2\pi} + \frac{\sup_{[h, +\infty[} |F'|}{\pi} \sqrt{I_2(\nu_1)(t)}. \end{aligned}$$

Proof. We see that

$$\begin{aligned} \mathcal{R}_1(X, F_h, \nu_1, \delta_{x=0})(t) &= \int_{\mathbb{R}} x \nu_1(x) \mathcal{H}(F_h \nu_1)(x) dx \\ &= \frac{1}{2\pi} \int_{\mathbb{R}} F_h(x') \nu_1(x') dx' \\ &\quad + \frac{1}{2\pi} \iint_{\mathbb{R}^2} x' \frac{F_h(x') - F_h(x)}{x - x'} \nu_1(x) \nu_1(x') dx' dx, \end{aligned}$$

hence,

$$\begin{aligned} \mathcal{R}_1(X, F_h, \nu_1, \delta_{x=0})(t) &= \frac{F_h(0)}{2\pi} + \frac{1}{2\pi} \int_{\mathbb{R}} (F_h(x') - F_h(0)) \nu_1(x') dx' \\ &\quad + \frac{1}{2\pi} \iint_{\mathbb{R}^2} x' \frac{F_h(x') - F_h(x)}{x - x'} \nu_1(x) \nu_1(x') dx' dx. \end{aligned}$$

Moreover, we notice that

$$-\frac{\sup_{[h, +\infty[} |F'|}{2\pi} \int_{\mathbb{R}} |x'| \nu_1(x') dx' \leq \frac{1}{2\pi} \int_{\mathbb{R}} (F_h(x') - F_h(0)) \nu_1(x') dx' \leq 0,$$

and

$$\left| \frac{1}{2\pi} \iint_{\mathbb{R}^2} x' \frac{F_h(x') - F_h(x)}{x - x'} \nu_1(x) \nu_1(x') dx' dx \right| \leq \frac{\sup_{[h, +\infty[} |F'|}{2\pi} \int_{\mathbb{R}} |x'| \nu_1(x') dx'.$$

Using the inequality

$$\int_{\mathbb{R}} |x'| \nu_1(x') dx' \leq \sqrt{I_2(\nu_1)(t)},$$

we end up with

$$\begin{aligned} & \frac{F_h(0)}{2\pi} - \frac{\sup_{[h, +\infty[} |F'|}{\pi} \sqrt{I_2(\nu_1)(t)} \\ & \leq \mathcal{R}_1(X, F_h, \nu_1, \delta_{x=0})(t) \leq \frac{F_h(0)}{2\pi} + \frac{\sup_{[h, +\infty[} |F'|}{2\pi} \sqrt{I_2(\nu_1)(t)}, \end{aligned}$$

which achieves the proof of Lemma 4.2. \square

Case 1: A simple analysis of the inequality

$$\frac{d}{dt} I_2(\nu_1)(t) \geq \underbrace{\left(1 - \frac{\chi F_h(0)}{2\pi}\right)}_{>0} - \frac{\chi \sup_{[h, +\infty[} |F'|}{2\pi} \sqrt{I_2(\nu_1)(t)},$$

ensures for $t \leq T$ the lower bound

$$I_2(\nu_1)(t) \geq \min \left(I_2(0), \left(\frac{2\pi}{\sup_{[h, +\infty[} |F'|} \left(1 - \frac{\chi F_h(0)}{2\pi}\right) \right)^2 \right).$$

Case 2: If $\chi > \chi^*$ the proof of the apparition of a singularity is similar to the one for the full model, see Proposition 1.1.

5 Some Estimates for (8) and (1) – (2)

In this section, we give what we consider to be key estimates to show the existence of solutions to the models we study.

5.1 Log type estimate and bound on the second moment for (8)

Proposition 5.1. *Let ν be a solution of (8). The following inequalities hold*

$$(31) \quad \frac{d}{dt} \int_{\mathbb{R}} \nu(x) \log \nu(x) dx = (\chi \|S\|_{\infty} - 1) \int_{\mathbb{R}} \frac{|\partial_x \nu(x)|^2}{\nu(x)} dx,$$

and

$$(32) \quad \frac{1}{2} \frac{d}{dt} \int_{\mathbb{R}} x^2 \nu(x) dx \leq 1 + \frac{\chi \|S\|_{\infty}}{2\pi} + \frac{\chi \|\partial_x S\|_{\infty}}{2\pi} \left(\int_{\mathbb{R}} x^2 \nu(x) dx \right)^{1/2}.$$

Proof. We differentiate in time $\int_{\mathbb{R}} \nu(x) \log \nu(x) dx$ and prove that it decreases. Since \mathcal{H} is an isometry on L^2 , see [27], we have

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \nu(x) \log \nu(x) dx &= - \int_{\mathbb{R}} \frac{|\partial_x \nu(x)|^2}{\nu(x)} dx - \chi \int_{\mathbb{R}} \mathcal{H}(S\nu)(x) \partial_x \nu(x) dx \\ &\leq - \int_{\mathbb{R}} \frac{|\partial_x \nu(x)|^2}{\nu(x)} dx + \chi \|\sqrt{\nu}\|_{\infty} \left\| \frac{\partial_x \nu}{\sqrt{\nu}} \right\|_2 \|\mathcal{H}(S\nu)\|_2 \\ &\leq - \int_{\mathbb{R}} \frac{|\partial_x \nu(x)|^2}{\nu(x)} dx + \chi \|\nu\|_{\infty}^{1/2} \left\| \frac{\partial_x \nu}{\sqrt{\nu}} \right\|_2 \|S\nu\|_2 \\ &\leq - \int_{\mathbb{R}} \frac{|\partial_x \nu(x)|^2}{\nu(x)} dx + \chi \|\nu\|_{\infty}^{1/2} \left\| \frac{\partial_x \nu}{\sqrt{\nu}} \right\|_2 \|S\|_{\infty} \|\nu\|_1^{1/2} \|\nu\|_{\infty}^{1/2}. \end{aligned}$$

Using next that $\|\nu\|_\infty \leq \|\partial_x \nu\|_1$ and that $\|\nu\|_1 = 1$, we obtain

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \nu(x) \log \nu(x) dx &\leq - \int_{\mathbb{R}} \frac{|\partial_x \nu(x)|^2}{\nu(x)} dx + \chi \left\| \frac{\partial_x \nu}{\sqrt{\nu}} \right\|_2 \|S\|_\infty \|\partial_x \nu\|_1 \\ &\leq - \int_{\mathbb{R}} \frac{|\partial_x \nu(x)|^2}{\nu(x)} dx + \chi \left\| \frac{\partial_x \nu}{\sqrt{\nu}} \right\|_2^2 \|S\|_\infty, \end{aligned}$$

hence (31).

In order to obtain equiintegrability, we need a bound on the second moment. We compute

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \int_{\mathbb{R}} x^2 \nu(x) dx &= 1 - \chi \int_{\mathbb{R}} x \nu(x) \mathcal{H}(S\nu)(x) dx \\ &= 1 - \frac{\chi}{2\pi} \iint_{\mathbb{R}^2} \frac{xS(y) - yS(x)}{x-y} \nu(x)\nu(y) dx dy \\ &= 1 - \frac{\chi}{2\pi} \iint_{\mathbb{R}^2} \left(S(y) + y \frac{S(y) - S(x)}{x-y} \right) \nu(x)\nu(y) dx dy \\ &\leq 1 + \frac{\chi \|S\|_\infty}{2\pi} - \frac{\chi}{2\pi} \iint_{\mathbb{R}^2} y \frac{S(y) - S(x)}{x-y} \nu(x)\nu(y) dx dy, \end{aligned}$$

hence (32) which provides an upper bound on $\int_{\mathbb{R}} x^2 \nu(x) dx$. Combining the two estimates (31) and (32), we obtain equiintegrability of the solution. \square

5.2 L^2 estimates for (8)

We prove L^2 type estimate for (8). Recall that the Hilbert transform maps L^4 to itself and that $C_4 > 0$ is a constant defined by (16).

Lemma 5.2. *Let ν be a solution of (8), with $\nu_0 \in L^2$. The following estimate holds*

$$(33) \quad \frac{d}{dt} \int_{\mathbb{R}} \frac{\nu(x)^2}{2} dx \leq -\frac{1}{4} \int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx + \chi C_4^2 \|S\|_\infty^4 \left(\int_{\mathbb{R}} \nu(x)^2 dx \right)^3.$$

Proof. Let us compute the derivative of $\int \nu^2 dx$:

$$\frac{d}{dt} \int_{\mathbb{R}} \nu(x)^2 dx = -2 \int_{\mathbb{R}} (|\partial_x \nu(x)|^2 + \chi \nu \partial_x \nu(x) \mathcal{H}(S\nu)(x)) dx,$$

which leads to

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \frac{\nu(x)^2}{2} dx &\leq -\frac{1}{2} \int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx + \frac{\chi}{2} \int_{\mathbb{R}} \nu(x)^2 |\mathcal{H}(S\nu)(x)|^2 dx \\ &\leq -\frac{1}{2} \int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx + \frac{\chi}{2} \|\nu\|_4^2 \|\mathcal{H}(S\nu)\|_4^2. \end{aligned}$$

Since \mathcal{H} maps L^4 to L^4 [27], we have

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \frac{\nu(x)^2}{2} dx &\leq -\frac{1}{2} \int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx + \chi \frac{C_4}{2} \|\nu\|_4^2 \|S\nu\|_4^2 \\ &\leq -\frac{1}{2} \int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx + \chi \frac{C_4}{2} \|S\|_\infty^2 \int_{\mathbb{R}} \nu(x)^4 dx. \end{aligned}$$

By the Cauchy-Schwarz inequality it comes

$$\int_{\mathbb{R}} \nu(x) |\partial_x \nu(x)| dx \leq \left(\int_{\mathbb{R}} \nu(x)^2 dx \right)^{1/2} \left(\int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx \right)^{1/2},$$

and from the Hölder inequality we deduce

$$\begin{aligned} \int_{\mathbb{R}} \nu(x)^4 dx &= -2 \int_{\mathbb{R}} \nu(x) \partial_x \nu(x) \left(\int_{-\infty}^x \nu(y)^2 dy \right) dx \\ &\leq 2 \left(\int_{\mathbb{R}} \nu(x) |\partial_x \nu(x)| dx \right) \left(\int_{\mathbb{R}} \nu(x)^2 dx \right), \end{aligned}$$

hence

$$\int_{\mathbb{R}} \nu(x)^4 dx \leq 2 \left(\int_{\mathbb{R}} \nu(x)^2 dx \right)^{3/2} \left(\int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx \right)^{1/2},$$

which yields that

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \frac{\nu(x)^2}{2} dx &\leq -\frac{1}{2} \int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx \\ &\quad + \chi C_4 \|S\|_{\infty}^2 \left(\int_{\mathbb{R}} \nu(x)^2 dx \right)^{3/2} \left(\int_{\mathbb{R}} |\partial_x \nu(x)|^2 dx \right)^{1/2}, \end{aligned}$$

hence (33) which will be useful for local existence on $(0, T)$. \square

5.3 L^2 estimates for (1) – (2)

We prove L^2 type estimate for (1) – (2).

Lemma 5.3. *Let (ν_1, ν_2) be a solution of (1) – (2). The following estimate holds*

$$(34) \quad \frac{d}{dt} \int_{\mathbb{R}} \nu_i(x)^2 dx \leq \|\partial_x \nu_i\|_2^2 (-2 + 6\chi C_4 \|S_j\|_{\infty}).$$

Proof. We derive the following estimates focusing on species i (with the convention $j \neq i$).

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \nu_i(x)^2 dx &= -2 \int_{\mathbb{R}} |\partial_x \nu_i(x)|^2 dx - 2\chi \int_{\mathbb{R}} \nu_i(x) \partial_x \nu_i(x) \mathcal{H}(S_j \nu_i)(x) dx \\ &\leq -2 \|\partial_x \nu_i\|_2^2 + 2\chi \|\partial_x \nu_i\|_2 \|\nu_i \mathcal{H}(S_j \nu_i)\|_2 \\ &\leq -2 \|\partial_x \nu_i\|_2^2 + 2\chi \|\partial_x \nu_i\|_2 \|\nu_i\|_4 \|\mathcal{H}(S_j \nu_i)\|_4 \\ &\leq -2 \|\partial_x \nu_i\|_2^2 + 2\chi C_4 \|\partial_x \nu_i\|_2 \|\nu_i\|_4^2 \|S_j\|_{\infty}. \end{aligned}$$

Using integration by parts, we can establish

$$\begin{aligned} \int_{\mathbb{R}} \nu_i(x)^4 dx &= - \int_{\mathbb{R}} \left(\int_{-\infty}^x \nu_i(y) dy \right) 3\nu_i(x)^2 \partial_x \nu_i(x) dx, \\ &\leq 3 \|\nu_i\|_4^2 \|\partial_x \nu_i\|_2 \int_{\mathbb{R}} |\nu_i(x)| dx, \end{aligned}$$

which leads to

$$\|\nu_i\|_4^2 \leq 3\|\nu_i\|_1\|\partial_x\nu_i\|_2 = 3\|\partial_x\nu_i\|_2,$$

since $\int_{\mathbb{R}} |\nu_i(x)| dx = 1$.

□

6 Proof of proposition 1.3

Define the function

$$g(x) = \frac{1}{1+x^2},$$

and recall the definition (27) of J_k for any function k

$$J_k(t) = \iint_{\mathbb{R}^2} k(x-y)\nu_1(t,x)\nu_2(t,y) dx dy.$$

The proof is essentially based on a bootstrap argument. We will establish the following points:

- as long as J_g is small enough, then $\|S_2\nu_1\|_1 = \|S_1\nu_2\|_1 = J_{F_h}$ keeps small,
- as long as $\|S_2\nu_1\|_1 = \|S_1\nu_2\|_1 = J_{F_h}$ keeps small, the L^2 norm of the solution decays towards 0,
- when the norms are small enough, (meaning the solution is already quite flat), then $\|S_2\nu_1\|_1 = \|S_1\nu_2\|_1 = J_{F_h}$ is small due to the smallness of the L^2 norm so that the decay to 0 is sustained.

The steps of the proof consists in defining thresholds leading us to the last point. We break the proof into several Lemmas.

Lemma 6.1. *For $i \in \{1, 2\}$, it holds that*

$$\mathcal{R}_i(g', F_h, \nu_1, \nu_2)(t) \leq \frac{3}{\pi} J_{F_h}(t) + \frac{\sup_{[h, +\infty[} |F'|}{2\pi} J_g(t).$$

Proof. This follows by injecting the following bounds, for all $x \in \mathbb{R}$,

$$\begin{aligned} |g'(x)| &\leq g(x), & g''(x) &\leq 8g(x), \\ \left| \frac{g'(z) - g'(z')}{z - z'} \right| &\leq 6(g(z) + g(z')). \end{aligned}$$

in Lemma 3.1.

□

We now state a result allowing to control J_{F_h} by J_g

Lemma 6.2. *For any $\varepsilon > 0$ there exists η (depending on F_h, ε) such that*

$$J_g \leq \eta \quad \Rightarrow \quad J_{F_h} \leq \varepsilon$$

Proof. For any $A > 0$ we compute

$$\begin{aligned}
J_{F_h}(t) &= \iint_{\mathbb{R}^2} F_h(x-y)\nu_1(x)\nu_2(y) \, dy \, dx \\
&= \iint_{|x-y|\leq A} F_h(x-y)\nu_1(x)\nu_2(y) \, dy \, dx + \iint_{|x-y|>A} F_h(x-y)\nu_1(x)\nu_2(y) \, dy \, dx \\
&\leq \sup_{[0,A]} \frac{F_h}{g} \iint_{|x-y|\leq A} g(x-y)\nu_1(x)\nu_2(y) \, dy \, dx \\
&\quad + \iint_{|x-y|>A} F_h(x-y)\nu_1(x)\nu_2(y) \, dy \, dx \\
&\leq J_g(t) \sup_{[0,A]} \frac{F_h}{g} + F_h(A).
\end{aligned}$$

Since $\lim_{x \rightarrow +\infty} F_h(x) = 0$, we can choose A such that $F_h(A) \leq \varepsilon/2$ and the conclusion follows for $\eta = \frac{\varepsilon}{2 \sup_{[0,A]} \frac{F_h}{g}}$. \square

Next, we compute the evolution of J_g .

Lemma 6.3. *Assume the solution of (1) – (2) exists until time $T > 0$. For all $t \leq T$, it holds that*

$$J_g(t) \leq J_g(0)e^{Ct},$$

where C is a constant that depends on F_h and χ .

Proof. We see that

$$\begin{aligned}
\frac{d}{dt} J_g(t) &= 2 \iint_{\mathbb{R}^2} g''(x-y)\nu_1(x)\nu_2(y) \, dy \, dx \\
&\quad - \chi \iint_{\mathbb{R}^2} g'(x-y) \left(\mathcal{H}(S_2\nu_1)(x) - \mathcal{H}(S_1\nu_2)(y) \right) \nu_1(x)\nu_2(y) \, dy \, dx.
\end{aligned}$$

With a few computations, we get

$$\begin{aligned}
&\iint_{\mathbb{R}^2} g'(x-y)\mathcal{H}(S_2\nu_1)(x)\nu_1(x)\nu_2(y) \, dy \, dx \\
&= \frac{1}{2\pi} \iiint\limits_{\mathbb{R}^4} \frac{g'(x-y)F_h(x'-y') - g'(x'-y)F_h(x-y')}{x-x'} \nu_1(x)\nu_2(y)\nu_1(x')\nu_2(y') \, dy' \, dx' \, dy \, dx \\
&= \frac{1}{2\pi} \iiint\limits_{\mathbb{R}^4} g'(x-y) \frac{F_h(x'-y') - F_h(x-y')}{x-x'} \nu_1(x)\nu_2(y)\nu_1(x')\nu_2(y') \, dy' \, dx' \, dy \, dx \\
&\quad + \frac{1}{2\pi} \iiint\limits_{\mathbb{R}^4} \frac{g'(x-y) - g'(x'-y)}{x-x'} F_h(x-y')\nu_1(x)\nu_2(y)\nu_1(x')\nu_2(y') \, dy' \, dx' \, dy \, dx \\
&\leq \frac{1}{2\pi} \left(\sup_{[h,+\infty[} |F'| J_{|g'|}(t) + 12\|F_h\|_\infty J_g(t) \right).
\end{aligned}$$

hence, using the symmetry for the second term, we obtain

$$\frac{d}{dt} J_g(t) \leq 2J_{g''}(t) + \frac{\chi}{\pi} \left(\sup_{[h,+\infty[} |F'| J_{|g'|}(t) + 12\|F_h\|_\infty J_g(t) \right)$$

thus,

$$(35) \quad J'_g(t) \leq C J_g(t).$$

with

$$C = 16 + \frac{\chi}{\pi} \left(\sup_{[h, +\infty[} |F'| + 12 \|F_h\|_\infty \right).$$

□

As a consequence, we have the following a priori estimate.

Lemma 6.4. *Assume the solution of (1) – (2) exists until time $T > 0$. Using notations of lemma 6.2, if $J_g(0)e^{-CT} \leq \eta$, then it holds that*

$$\sup_{[0, T]} \|S_2 \nu_1\|_1 = \sup_{[0, T]} \|S_1 \nu_2\|_1 = \sup_{[0, T]} \iint_{\mathbb{R}^2} F_h(x-y) \nu_1(x) \nu_2(y) \, dy \, dx \leq \varepsilon.$$

The strategy now is to establish the smallness of J_h using the flatness of ν_i measured in terms of the smallness of $\nu_i|_2$

Lemma 6.5. *It holds that*

$$\|S_2 \nu_1\|_2 \leq \sqrt{\|\nu_1\|_\infty} \sqrt{J_{F_h}}.$$

Furthermore, for every $\varepsilon > 0$, there exists η_2 (depending on F_h, ε), such that

$$(36) \quad \|\nu_2\|_2 \leq \eta_2 \quad \Rightarrow \quad J_{F_h} \leq \|S_2\|_\infty \leq \varepsilon.$$

Proof. The inequality follows from $\|S_2 \nu_1\|_2 \leq \|S_2\|_\infty \|\nu_1\|_2$, $\|S_2\|_\infty \leq F_h(0) = 1$, by construction, Holder's inequality and $\|\nu_1\|_1 = 1$.

We only need to prove the last assertion. Define the set $A_\varepsilon(x)$ by

$$A_\varepsilon(x) = \left\{ y, F_h(x-y) \geq \frac{\varepsilon}{2} \right\}.$$

Due to translation invariance, we notice that the measure $|A_\varepsilon(x)|$ does not depend on x . Moreover, we see that

$$\begin{aligned} S_2(t, x) &= \int_{\mathbb{R}} F_h(x-y) \nu_2(t, y) \, dy \\ &= \int_{A_\varepsilon(x)} F_h(x-y) \nu_2(t, y) \, dy + \int_{\mathbb{R} \setminus A_\varepsilon(x)} F_h(x-y) \nu_2(t, y) \, dy, \\ &\leq \|\nu_2\|_2 \sqrt{|A_\varepsilon|} + \frac{\varepsilon}{2}, \end{aligned}$$

we end up by choosing $\eta_2 \leq \frac{\varepsilon}{2\sqrt{|A_\varepsilon|}}$.

□

Therefore, one needs now to prove that ν_1 gets small in L^2 . Thus, we differentiate $\int_{\mathbb{R}} \nu_1(x)^2 dx$ (computations are identical for ν_2)

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \nu_1(x)^2 dx &= -2 \int_{\mathbb{R}} (|\partial_x \nu_1(x)|^2 + \chi \nu_1(x) \partial_x \nu_1(x) \mathcal{H}(S_2 \nu_1)(x)) dx \\ &\leq -2 \|\partial_x \nu_1\|_2^2 + 2\chi \|\partial_x \nu_1\|_2 \|\nu_1\|_{\infty} \|\mathcal{H}(S_2 \nu_1)\|_2, \end{aligned}$$

hence recalling (16), with $C_2 = 1$, we obtain

$$(37) \quad \frac{d}{dt} \int_{\mathbb{R}} \nu_1(x)^2 dx \leq -2 \|\partial_x \nu_1\|_2^2 + 2\chi \|\partial_x \nu_1\|_2 \|\nu_1\|_{\infty} \|S_2 \nu_1\|_2.$$

We use now this result in inequality (37). We first see that

$$\frac{d}{dt} \int_{\mathbb{R}} \nu_1(t, x)^2 dx \leq -2 \|\partial_x \nu_1\|_2^2 + 2\chi \|\partial_x \nu_1\|_2 \|\nu_1\|_{\infty}^{3/2} \|S_2\|_{\infty}.$$

Computing formally

$$\nu_1(t, x)^{3/2} = \int_{-\infty}^x \frac{3}{2} \nu_1(t, y)^{1/2} \partial_x \nu_1(t, y) dy,$$

and recalling that $\|\nu_1\|_1 = 1$, we obtain

$$\|\nu_1\|_{\infty}^{3/2} \leq \frac{3}{2} \|\partial_x \nu_1\|_2,$$

hence the estimate

$$(38) \quad \frac{d}{dt} \int_{\mathbb{R}} \nu_1(t, x)^2 dx \leq (-2 + 3\chi \|S_2\|_{\infty}) \|\partial_x \nu_1\|_2^2.$$

This leads to the statement of the L^2 bootstrap.

Lemma 6.6. *Using notations of Lemma 6.5. Assume $\varepsilon > 0$, is such that $3\chi\varepsilon < 1$, and $\|\nu_{1,0}\|_2, \|\nu_{2,0}\|_2 \leq \eta_2$, then for all $t > 0$*

$$\frac{d}{dt} \|\nu_i\|_2 \leq 0,$$

and

$$\int_{\mathbb{R}} \nu_i(x)^2 dx \leq \frac{1}{\left(\frac{2t}{C_{Nash}} + \left(\frac{1}{\int \nu_i^2(0)} \right)^2 \right)^{\frac{1}{2}}},$$

where C_{Nash} is the constant in the Nash inequality

$$\|\nu_i\|_2^6 \leq C_{Nash} \|\partial_x \nu_i\|_2^2 \|\nu_i\|_1^4$$

Proof. The proof is based on a bootstrap argument. Firstly, as long as it holds that $\|\nu_1\|_2, \|\nu_2\|_2 \leq \eta_2$, we have $-2 + 3\chi\|S_j\|_\infty \leq -1$. Indeed, using (36), we deduce that $\|S_i\|_\infty \leq \varepsilon$. Hence, from (38), it follows that

$$\frac{d}{dt} \int_{\mathbb{R}} \nu_i(t, x)^2 dx \leq - \int_{\mathbb{R}} (\partial_x \nu_i(x))^2 dx \leq 0.$$

And thereby the L^2 norm decay so that $\|n\nu_i\|_2 \leq \eta_2$ and $3\chi\|S_j\|_\infty \leq -1$ keep propagated.

Furthermore, using Nash inequality

$$\|\nu_i\|_2^6 \leq C_{Nash} \|\partial_x \nu_i\|_2^2 \|\nu_i\|_1^4 = C_{Nash} \|\partial_x \nu_i\|_2^2.$$

In addition, we can quantify the decay. Indeed, combining the inequalities, we have

$$\frac{d}{dt} \int_{\mathbb{R}} \nu_i(t, x)^2 dx \leq - \int_{\mathbb{R}} (\partial_x \nu_i(x))^2 dx \leq - \frac{1}{C_{Nash}} \left(\int_{\mathbb{R}} \nu_i(x)^2 dx \right)^3,$$

leading to the estimate

$$\int_{\mathbb{R}} \nu_i(t, x)^2 dx \leq \frac{1}{\sqrt{\frac{2t}{C_{Nash}} + \left(\frac{1}{\int_{\mathbb{R}} \nu_i^2(t=0, x) dx} \right)^2}}$$

□

We need now to establish that for small initial values of $J_g(t=0)$, we reach the condition of the L^2 bootstrap as described in lemma 6.6. For this, we go back to estimate (37). We use an alternative majoration of $\|S_2\nu_1\|_2$:

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}} \nu_1(t, x)^2 dx &\leq -2\|\partial_x \nu_1\|_2^2 + 2\chi\sqrt{F_h(0)}\|\partial_x \nu_1\|_2\|\nu_1\|_\infty^{3/2}\|S_2\nu_1\|_1 \\ &= -2\|\partial_x \nu_1\|_2^2 + 2\chi\|\partial_x \nu_1\|_2\|\nu_1\|_\infty^{3/2}\|S_2\nu_1\|_1 \\ &\leq -2\|\partial_x \nu_1\|_2^2 + 3\chi\|\partial_x \nu_1\|_2^2\|S_2\nu_1\|_1. \end{aligned}$$

The bootstrap argument is now the following: we fix $0 < \varepsilon \leq \frac{1}{3\chi}$ (which value will be precised later) and use the previous notations $\eta_1(\varepsilon), \eta_2(\varepsilon)$. We consider a parameter $T > 0$ to be defined later.

- We assume $J_g(0) \leq \eta_1(\varepsilon)e^{-CT}$, where C is the constant in lemma 3.2. Therefore $\sup_{[0, T]} J_g \leq J_g(0)e^{CT} \leq \eta_1$,
- in particular, by lemma 6.2, we have $\|S_i\|_\infty = J_{F_h} \leq \varepsilon$ for $t \in [0, T]$,
- therefore, the L^2 norm of the solution are decaying on intervall $[0, T]$, as stated in lemma 6.6, and we have especially

$$\int_{\mathbb{R}} \nu_i(t, x)^2 dx \leq \frac{1}{\sqrt{\frac{2t}{C_{Nash}} + \left(\frac{1}{\int_{\mathbb{R}} \nu_i^2(t=0, x) dx} \right)^2}}, \quad t \in]0, T].$$

- Finally, we choose $T > 0$ such that

$$\sqrt{\frac{C_{Nash}}{2T}} \leq \eta_2,$$

- this ensures that after time T , the decay is preserved by lemma 6.6

Alltogether, this leads to the results that if either $J_g(0) \leq \eta_1 e^{-CT}$ or $\|\nu_i\|_2 \leq \eta_2$ ($i = 1, 2$), then we have global existence and algebraic decay of the L^2 norm of the solution. This ends the proof of proposition 1.3.

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