Analysis of a nonlocal and nonlinear system for cell-cell communication

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Abstract

We consider a system of two nonlocal and nonlinear partial differential equations that describe some aspects of yeast cell-cell communication. We study local and global existence and uniqueness of solutions. We consider mild solutions and we perform bilinear and trilinear fixed point arguments in suitable functional spaces.

Keywords: Existence problems for PDEs: global existence, local existence; cell communication and cell polarization.
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1 Introduction

Cell-cell communication is crucial for many biological phenomena such as cell migration, axon guidance *e.g.* some cell-cell communication does not require direct cell-cell contact and is mediated by a pheromone that diffuses into the intercellular space and binds to receptors on the cell surface. In this work we study two models, initially introduced in [15, 16, 5, 7, 8], that describe some aspects of single yeast cell polarization and cell-cell communication in the context of yeast mating. The first model describes the polarization of a single cell subjected to a pheromone concentration

$$\begin{cases} \partial_t n(t,x) = D\partial_{xx} n(t,x) + \partial_x \Big(\chi * n\mathcal{H}(Sn)\Big)(t,x), \\ n(0,x) = n_0(x). \end{cases} \tag{1.1}$$

Here χ, S, $n : [0,+\infty[\times\mathbb{R} \longrightarrow \mathbb{R}$ are real valued functions, $\mathcal{H}$ is the Hilbert transform defined in the Fourier level by the formula $\widehat{\mathcal{H}(f)}(\xi) = -i\frac{\xi}{|\xi|}\widehat{f}(\xi)$, $D > 0$ is the diffusion coefficient, $n_0 : \mathbb{R} \longrightarrow \mathbb{R}$ and $*$ is the usual convolution product.

Briefly, the main assumptions leading to (1.1) are the following: the cell is represented by the half-space $\mathbf{H} = \mathbb{R}\times]0,+\infty[$ and its membrane is the real line. We denote by $n(t,x)$ the concentration of proteins (or markers) involved in the polarization process (*e.g. Cdc42* protein) that are trapped at the boundary. The nonlocal nonlinearities in (1.1) describe positive feedback loops involved in the dynamics of polarization markers: molecular markers not only diffuse in the cytoplasm of the cell, but are also actively transported by molecular motors along the filaments

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of the cytoskeleton, whose dynamic organization is regulated by the markers themselves, by an external signal noted S. Moreover in (1.1) the function χ accounts for the mobility (depending on time and space) of the membrane markers to describe mobile surface polarity patch and for the yeast cell cycle [14].

When χ and S are constant, it is known that (1.1) exhibits pattern formation (either a blow-up or a convergence to a non-homogeneous steady state) under certain conditions, see [6, 4]. Our goal here is to extend the well-posedness study to the case where χ and S are functions of space and time.

Next, following ideas given in [15, 7, 8], we study the well-posedness of the coupled system that allows to describe some aspects of cell-cell communication:

$$\begin{cases} \partial_t n_1(t,x) = D_1 \partial_{xx} n_1(t,x) + \partial_x\big(\chi_1 * n_1 \mathcal{H}(S_2 n_1)\big)(t,x), \\ \partial_t n_2(t,x) = D_2 \partial_{xx} n_2(t,x) + \partial_x\big(\chi_2 * n_2 \mathcal{H}(S_1 n_2)\big)(t,x), \\ n_1(0,x) = n_{1,0}(x) \qquad \text{and} \qquad n_2(0,x) = n_{2,0}(x), \end{cases} \tag{1.2}$$

where $n_1, n_2, \chi_1, \chi_2 : [0,+\infty[\times\mathbb{R} \longrightarrow \mathbb{R}$ are real valued functions, $D_i > 0$ are the diffusion coefficients, the functions S_1, S_2 are given by the expression

$$S_1(t,x) = K_1 * n_1(t,x) \qquad \text{and} \qquad S_2(t,x) = K_2 * n_2(t,x), \tag{1.3}$$

with K_1, K_2 belonging to $L^2(\mathbb{R})$ and depending on the distance h between the two cell membranes see Figure 1.

In short, in (1.2) – (1.3) the two cell membranes are modeled as two parallel lines separated by a distance h from each other (see Figure 1 below). On each cell membrane, proteins, with density $n_i(t,x)$, can either diffuse freely or be actively transported to regions with high concentrations of protein and external signal (S_i) produced by the opposite cell type. Moreover, space and time variable mobilities (χ_i) serve both as sites of pheromone secretion and pheromone perception. We refer to Section 2 for a detailed presentation of the model with biological motivations.

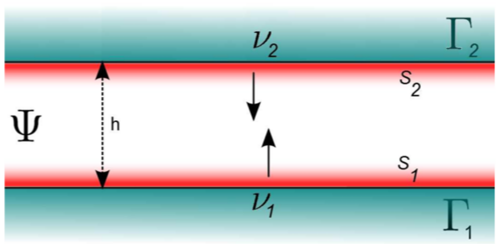

Figure 1: Tangential model for the communication between two cells

Note that the total molecular contents, $M_i := \displaystyle\int_{\mathbb{R}} n_i(t,x)\,\mathrm{d}x$, are conserved for each cell in (1.2) and also in (1.1).

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, let us briefly comment the literature. When χ and S are constant, the problem (1.1) is similar to the Modified Keler-Segel (MKS) [6]. In such a case, it was proved that above a critical value of χ or S 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) and with constant coefficients χ and S.

In terms of modeling, the polarization of a cell occurs when a singularity appears in (1.1). In this case, the membrane markers concentrate in one small region, which is the signature of polarization. Similarly, a necessary condition for a dialogue between cells to take place (leading to the mating between the two cells) is the appearance of a singularity in (1.2). In this work, we perform a mathematical analysis of (1.1) and (1.2) which provides criteria to prevent cell polarization and dialogue between cells. These criteria depend on the biological ingredients of the model (χ_i, S_i, K_i) and correspond to the biological observations. This mathematical analysis is a first step towards a better understanding of the strategy that use yeast cells during pairing.

In the present work we first study local well-posedness for (1.1) for general functions $\chi \in L^\infty_t(L^1_x)$ and $S \in L^\infty_t(L^\infty_x)$. For simplicity, we assume that $D = 1$ in (1.1). To do so, we consider mild solutions (via the Duhamel formula) in appropriate functional spaces, and although many different functional spaces can be considered, for simplicity, we work in Lebesgue and Sobolev spaces (see Section 3 below for precise definitions).

Theorem 1 (Local in time mild solutions for (1.1))**.** *Assume $n_0 \in L^2(\mathbb{R})$, $\chi \in L^\infty_t(L^1_x)$ and $S \in L^\infty_t(L^\infty_x)$. Equation (1.1) admits a unique mild solution in $L^\infty([0,T_0], L^2(\mathbb{R}))$, with $T_0 > 0$, of the form*

$$n(t,x) = h_t * n_0(x) + \int_0^t h_{t-s} * \left[\partial_x\Big(\chi * n\mathcal{H}(Sn)\Big)\right](s,x)\,\mathrm{d}s, \tag{1.4}$$

where h_t is the one-dimensional heat kernel.

Next, we show that some local well-posedness results can be extended to the system (1.2) – (1.3). For simplicity, again, we assume that $D_i = 1$ in (1.2). To do so, define the vectorial quantities

$$\vec{\theta}_0(x) = \begin{bmatrix} n_{1,0}(x) \\ n_{2,0}(x) \end{bmatrix} \quad \text{and} \quad \vec{\theta}(t,x) = \begin{bmatrix} n_1(t,x) \\ n_2(t,x) \end{bmatrix}, \tag{1.5}$$

$$\vec{\mathbb{S}}_{[\vec{\theta}]}(t,x) = \begin{bmatrix} \chi_1 * n_1\mathcal{H}(S_2 n_1) \\ \chi_2 * n_2\mathcal{H}(S_1 n_2) \end{bmatrix}(t,x). \tag{1.6}$$

The system (1.2) can be rewritten as

$$\begin{cases} \partial_t\vec{\theta}(t,x) = \partial_{xx}\vec{\theta}(t,x) + \partial_x\vec{\mathbb{S}}_{[\vec{\theta}]}(t,x), \\ \vec{\theta}(0,x) = \vec{\theta}_0(x), \end{cases} \tag{1.7}$$

whose integral (vectorial) representation is (via Duhamel's formula):

$$\vec{\theta}(t,x) = h_t * \vec{\theta}_0(x) + \int_0^t h_{t-s} * \partial_x\vec{\mathbb{S}}_{[\vec{\theta}]}(s,x)\,\mathrm{d}s. \tag{1.8}$$

Theorem 2 (Local in time mild solutions for system (1.8))**.** *Assume $\vec{\theta}_0 \in L^2(\mathbb{R})$, $\chi_1, \chi_2 \in L^\infty_t(L^1_x)$ and $K_1, K_2 \in L^2(\mathbb{R})$. There exists a time $T_0 > 0$ such that equation (1.8) admits a mild solution $\vec{\theta}(t,x)$ in $L^\infty([0,T_0], L^2(\mathbb{R}))$.*

Remark 1.1. *In Theorem 1, the existence time T_0 depends on the L^2 norm of the initial data and of the L^∞ norm of S (see (4.32)). In Theorem 2, it depends on the L^2 norms of the initial data and the kernels K_1, K_2 that define the functions S_1, S_2 (see (4.35)).*

To obtain global solutions we still look for mild solutions via a Banach-Picard fixed point algorithm. However, the space $L_t^\infty(L_x^2)$ no longer seems to be suitable for this new purpose. Instead, we consider the functional space $E = L_t^\infty(L_x^2) \cap L_t^2(\dot{H}_x^1)$ which captures different information using homogeneous Sobolev spaces (see Section 3 below for a precise definition of this space).

Theorem 3 (Global Existence for the bilinear equation (1.1))**.** *Assume $n_0 \in L^2(\mathbb{R})$, $\chi \in L^2([0, +\infty[, L^2(\mathbb{R}))$ and $S \in L^\infty([0, +\infty[, L^\infty(\mathbb{R}))$. There exists a small positive constant $\mathfrak{C}$ such that if*

$$\|n_0\|_{L^2} \|\chi\|_{L_t^2(L_x^2)} \|S\|_{L_t^\infty(L_x^\infty)} \leq \mathfrak{C}, \tag{1.9}$$

then system (1.1) admits a unique global mild solution in $L^\infty([0, +\infty], L^2(\mathbb{R})) \cap L^2([0, +\infty], \dot{H}^1(\mathbb{R}))$ of the form

$$n(t, x) = h_t * n_0(x) + \int_0^t h_{t-s} * \left[\partial_x \Big(\chi * n\mathcal{H}(Sn) \Big) \right] (s, x) \, \mathrm{d}s. \tag{1.10}$$

Theorem 4 (Global existence for the trilinear system (1.2))**.** *Assume $\vec{\theta}_0 \in L^2(\mathbb{R})$, $\chi_1, \chi_2 \in L^2([0, +\infty[, L^2(\mathbb{R}))$ and $K_1, K_2 \in L^2(\mathbb{R})$. There exists a small positive constant $\mathfrak{C}$ such that if*

$$\|\vec{\theta}_0\|_{L^2}^2 (\|\chi_1\|_{L_t^2(L_x^2)} \|K_1\|_{L^2} + \|\chi_2\|_{L_t^2(L_x^2)} \|K_2\|_{L^2}) < \mathfrak{C}, \tag{1.11}$$

then (1.2) has a unique global mild solution in the space $L^\infty([0, +\infty], L^2(\mathbb{R})) \cap L^2([0, +\infty], \dot{H}^1(\mathbb{R}))$.

Let us make a few comments. In Theorems 1 and 2, we use a fixed point argument and if we consider very large initial data, then the existence time will be very small. In Theorems 3 and 4, although based on the same general arguments, no relation between the size of the initial data and the existence time is necessary. Thus, under these conditions global solutions can be considered, but only for *small* initial data. To the best of our knowledge, the existence of global in time mild solutions with *large* initial data is out of reach for the moment.

Apart from the two cases mentioned here, we leave the existence of mild solutions, and in particular blow-up criteria, for problems (1.1) and (1.2) – (1.3) as open problems and we refer to [8] for preliminary answers for classical solutions.

The present paper is organized as following. In Section 2, we recall the biological justifications of (1.1) and (1.2) – (1.3). In Section 3 we give some notations and results that will be used in the proofs. In Section 4 we prove Theorems 1 and 2. In Section 5 we prove Theorems 3 and 4.

2 Model construction

In this section we recall the biological justification of equation (1.1) in the context of yeast cell polarization. Next, we detail the construction of the coupled model (1.2) – (1.3).

2.1 A validated model for the polarization of yeast cells

Cell polarization is the process by which a cell transitions from a spherically symmetric shape to a state with a preferred axis [1, 17, 16, 19, 20]. The molecular pathways involved in cell polarization have been studied experimentally in some detail over the past decade, see [14] for a recent review in the context of yeast cell mating. The results suggest that the small

GTPase *Cdc42* and its scaffold, the *Bem1* protein, are involved during the polarization process. Moreover, it is known [22, 16], that the dynamics of *Cdc42* depend on the dynamics of the cytoskeleton filaments. The cellular cytoskeleton is a network of long semi-flexible filaments made of protein subunits [18]. 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 [22], it has been proposed that yeast polarization relies on a positive feedback loop in the dynamics of polarity markers, which is mediated by the actin cytoskeleton. 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.

According to the previous considerations, in [15, 5, 16, 7], a model based on partial differential equation was used and studied to describe yeast polarization. Suppose the cell is represented by the half-space $\mathbf{H} = \mathbb{R}\times]0,+\infty[$ with $\mathbf{x} = (x, y)$ as spatial variable. Denote by $\nu(t,\mathbf{x})$ the concentration in the cytoplasm of proteins (or markers) involved in cell polarization, by $n(t, x)$ 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 [16] is:

$$\partial_t\nu(t,\mathbf{x}) = D\Delta\nu(t,\mathbf{x}) - \chi\nabla\cdot(\nu(t,\mathbf{x})\nabla c(t,\mathbf{x})) , \quad t>0 , \quad \mathbf{x}\in\mathbf{H} , \tag{2.12}$$

completed by the flux boundary condition:

$$D\partial_y\nu(t,x,0) - \chi\nu(t,x,0)\partial_y c(t,x,0) = -\partial_t n(t,x) , \quad x\in\mathbb{R} , \tag{2.13}$$

where $\chi > 0$.

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 $n(t, x)$ is

$$\partial_t n(t,x) = k_{\text{on}}\,\nu(t,x,0) - k_{\text{off}}\,\mu(t,x) . \tag{2.14}$$

In this model, the 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 with density S. After a dimensional analysis, the model that describes the density of actin filaments is

$$\begin{cases} -\Delta c(t,\mathbf{x}) = 0, & \mathbf{x}\in\mathbf{H} , \\ \partial_z c(t,x,0) = S(t,x)\mu(t,x), & x\in\mathbb{R} . \end{cases} \tag{2.15}$$

2.2 Heuristic justification of the use of the Hilbert transform in (1.1)

The Hilbert transform of a function $f\in L^p(\mathbb{R})$, $1\le p<+\infty$ is defined as the Cauchy principle value integral [21]

$$\mathcal{H}(f)(x) = \frac{1}{\pi} p.v. \int_{\mathbb{R}} \frac{f(y)}{x-y}\,\mathrm{d}y . \tag{2.16}$$

Obviously, the integral (2.16) exists for almost all x. We define the function P by

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

and the Poisson kernel by

$$P_\varepsilon(x) = \frac{1}{\varepsilon}P\left(\frac{x}{\varepsilon}\right) , \tag{2.17}$$

with $\varepsilon > 0$. 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

$$\forall (x,y) \in \mathbb{R} \times \mathbb{R}_+ , \quad Q_y(x) = \frac{1}{y} Q\left(\frac{x}{y}\right) , \tag{2.18}$$

with

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

As usual, $\mathcal{S}(\mathbb{R})$ is the Schwartz space function, defined as the space of all functions $f \in \mathcal{C}^\infty(\mathbb{R})$ such that

$$\forall (\alpha, \beta) \in \mathbb{N}^2 , \quad \sup_{x\in\mathbb{R}} |x^\alpha f^{(\beta)}(x)| < +\infty ,$$

and $\mathcal{S}'(\mathbb{R})$ denotes its dual space.

Theorem 5 (Stein [21], Chapter III)**.** *The convergence holds*

$$Q_y \to \mathcal{H} \text{ in } \mathcal{S}' \text{ as } y \to 0 .$$

The link between the Hilbert transform and the conjugate of the Poisson kernel explains why, in (2.15) the passage from the normal derivative of c at $z = 0$ to its tangential derivative at $z = 0$, involves the Hilbert transform.

Lemma 2.1. *The solution of* (2.15) *is*

$$c(t,x,z) = -\frac{1}{\pi} \int_{x'\in\mathbb{R}} \log\left(\sqrt{(x-x')^2+z^2}\right) S(t,x')n(t,x')\,\mathrm{d}x' , \tag{2.19}$$

and it holds that

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

Proof. We first verify that such a function c is solution to (2.15). We compute

$$\begin{aligned} \partial_x c(t,x,z) &= -\frac{1}{\pi} \int_{x'\in\mathbb{R}} \frac{x-x'}{(x-x')^2+z^2} S(t,x')n(t,x')\,\mathrm{d}x' \\ &= -\left(Q_z * Sn(t,\cdot)\right)(x) , \end{aligned}$$

where Q_z is defined by (2.18), and

$$\partial_{xx} c(t,x,z) = -\frac{1}{\pi} \int_{x'\in\mathbb{R}} \frac{-(x-x')^2+z^2}{((x-x')^2+z^2)^2} S(t,x')n(t,x')\,\mathrm{d}x' .$$

Furthermore, recalling the definition of the Poisson kernel (2.17) we have

$$\begin{aligned} \partial_z c(t,x,z) &= -\frac{1}{\pi} \int_{x'\in\mathbb{R}} \frac{z}{(x-x')^2+z^2} S(t,x')n(t,x')\,\mathrm{d}x' \\ &= -\left(P_z * Sn(t,\cdot)\right)(x) , \end{aligned}$$

and

$$\partial_{zz} c(t,x,z) = -\frac{1}{\pi} \int_{x'\in\mathbb{R}} \frac{(x-x')^2-z^2}{((x-x')^2+z^2)^2} S(t,x')n(t,x')\,\mathrm{d}x' ,$$

hence

$$\Delta c(t,x,z) = 0 .$$

Since the Poisson kernel is an approximation of the unity, we deduce

$$\lim_{z\to 0} \partial_z c(t,x,z) = \partial_z c(t,x,0) = \lim_{z\to 0} \left(-P_z * Sn(t,\cdot)\right)(x) = -S(t,x)n(t,x)\,.$$

Using Theorem 5, it follows that

$$\lim_{z\to 0} \partial_x c(t,x,z) = \partial_x c(t,x,0) = \lim_{z\to 0} \left(-Q_z * Sn(t,\cdot)\right)(x) = -\mathcal{H}(Sn)(t,x)\,.$$

Lemma 2.1 is thus proven. □

In the supercritical case, *i.e.*, numerical simulations [5, 3], suggest that the solution $\nu(t,\mathbf{x})$ of (2.12) – (2.15) concentrates on the boundary $\{y=0\}$. Assuming that $\nu(t,x,y) = n(t,x)\delta(y=0)$, we can formally write the dynamics of $n(t,x)$ as follows:

$$\partial_t n(t,x) = \partial_{xx} n(t,x) + \chi \partial_x \left(n\,\mathcal{H}(Sn)\right)(t,x) \qquad t>0\,, x\in\mathbb{R}\,. \tag{2.20}$$

In this work we modify (2.20) into (1.1) in order to add a nonlocal effect.

2.3 Link between (1.1) and the MKS system

In the case where $\chi > 0$ is a constant, there is a link between (2.20) and the so-called modified Keller-Segel system [4] (MKS):

$$\begin{cases} \partial_t n(t,x) = \partial_{xx} n(t,x) - \chi \partial_x \left(n(t,x)\partial_x c(t,x)\right) & t>0\,, x\in\mathbb{R}\,, \\ c(t,x) = K * n(t,x) \quad t>0\,, x\in\mathbb{R}\,, \\ n(t=0,x) = n_0(x) \quad x\in\mathbb{R}\,, \end{cases} \tag{2.21}$$

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

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

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

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

from which we deduce

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

□

Using Lemma 2.2, we see that (2.21) rewrites as (1.1).

2.4 Boundary model (1.2) – (1.3) 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), see Figure 2, and carry a pheromone receptor to detect the pheromone produced by cells of the opposite type, [10]. Following [15, 7], we study 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, [12, 1, 19, 20, 14], we assume that the pheromone contributes to the nucleation of new filaments at the membrane of the opposite type cell, see Figure 2 below.

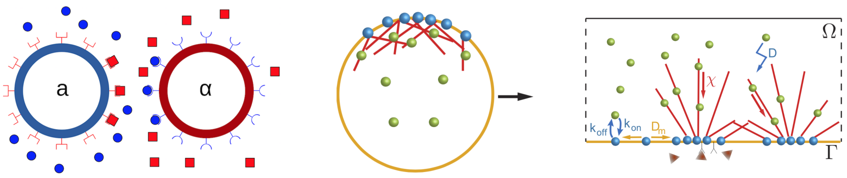

Figure 2: Model for yeast cell communication. On the left, yeast cells of both types secrete some pheromone ($\mathbf{a}$ or α) and bear a pheromone receptor to detect the pheromone produced by the cells of the opposite type. On the middle and on the right a two-dimensional model of protein dynamics 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.

This additional level of pairwise cell communication leads to the following rectification of the model (1.1): for the $\#i$ cell, we consider the advection field to be $\chi_i \mathcal{H}(S_j \nu_i)$ 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:

$$\partial_t \nu_i(t,x) = \partial_{xx}\nu_i(t,x) + \partial_x\Big(\nu_i(t,x)\mathcal{H}\left(S_j(t,x,h)\nu_i(t,x)\right)\Big), \tag{2.22}$$

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

$$\begin{cases} -\Delta S_j + \lambda S_j = 0\,, & \text{on } \Psi\,, \\ \nabla S_j \cdot \mathbf{e}_j = -\nu_j\,, & \text{on } \Gamma_j\,, \end{cases} \tag{2.23}$$

where $\mathbf{e}_1 = -\mathbf{e}_2$ denotes the unit outward normal vector to Γ_j. The solution of (2.23) can be explicitly computed: for all $t > 0$ and $x \in \mathbb{R}$, one has

$$S_j(t,x,h) = \frac{1}{\pi}\int_{\mathbb{R}} F(\sqrt{(x-x')^2+h^2})\,\nu_j(t,x')\,\mathrm{d}x'\,, \tag{2.24}$$

where F is the Bessel potential

$$F(r) = \frac{1}{4\pi}\int_0^{+\infty} \frac{e^{-\lambda z - \frac{r^2}{4z}}}{z}\,\mathrm{d}z\,. \tag{2.25}$$

3 Notations

We gather here some notation and some material that will be used in the sequel.

- If $f : [0, +\infty[\times\mathbb{R} \longrightarrow \mathbb{R}$ is a real valued measurable function, for $1 \leq p, q \leq +\infty$ we will denote by $L^p_t(L^q_x)$ the L^p(in time)-L^q(in space) Lebesgue space which is given by the condition
$$\|f\|_{L^p_t(L^q_x)} = \left(\int_0^{+\infty} \|f(t,\cdot)\|^p_{L^q}\, \mathrm{d}t\right)^{\frac{1}{p}} < +\infty,$$
with the usual modifications when $p = +\infty$ or $q = +\infty$.

- For $t > 0$, the heat kernel is given by the function $h_t(x) = \frac{1}{\sqrt{4\pi t}} e^{-\frac{|x|^2}{4t}}$ for which we have the estimates
$$\|\partial^k_x h_t\|_{L^p} \leq Ct^{-\frac{k+(1-1/p)}{2}}, \tag{3.26}$$
with $k \in \mathbb{N}$ and $1 \leq p \leq +\infty$.

- The homogeneous Sobolev spaces $\dot{H}^1(\mathbb{R})$ is given as the set of tempered distributions (modulo polynomials) such that
$$\|f\|_{\dot{H}^1(\mathbb{R})} = \|\partial_x f\|_{L^2} \simeq \left(\int_{\mathbb{R}} |\xi|^2 |\widehat{f}(\xi)|^2\, \mathrm{d}\xi\right)^{\frac{1}{2}} < +\infty.$$

- The homogeneous Sobolev space $\dot{H}^{-1}(\mathbb{R})$ can be defined by duality with respect to the space $\dot{H}^1(\mathbb{R})$, but it can also be characterized by the following condition in the Fourier variable
$$\|f\|_{\dot{H}^{-1}(\mathbb{R})} \simeq \left(\int_{\mathbb{R}} |\xi|^{-2} |\widehat{f}(\xi)|^2\, \mathrm{d}\xi\right)^{\frac{1}{2}} < +\infty.$$

4 Local Solutions

We study here local in time solutions for the equations (1.1) and (1.2) and for this we will consider mild solutions (via the Duhamel formula) in suitable functional spaces. Although many different functional spaces can be considered, for the sake of simplicity we will work in the space $L^\infty_t(L^2_x)$.

4.1 Proof of Theorem 1.

Here we study the existence of local Solutions for the bilinear system (1.1). Let us recall that the Banach-Picard fixed point theorem allows us to obtain a solution to equations of the form
$$n = e_0 + B(n, n), \tag{4.27}$$
where e_0 is an initial data and $B(\cdot, \cdot)$ is a bilinear application. Indeed, if we fix a Banach space $(E, \|\cdot\|_E)$ and if we have the estimates
$$\|e_0\|_E \leq \delta, \qquad \|B(n, n)\|_E \leq C_B \|n\|_E \|n\|_E, \tag{4.28}$$
then we only need to verify the condition
$$\delta < \frac{1}{4C_B}, \tag{4.29}$$

to obtain a unique solution of the equation (4.27). See [11, Theorem 5.1] for a proof of this bilinear version of the Banach-Picard fixed point theorem.

In the particular case of equation (1.4) above -which is already in the form of equation (4.27)- we will consider the Banach space $E = L^\infty([0,T], L^2(\mathbb{R}))$ endowed with the norm

$$\|f\|_{L^\infty_t(L^2_x)} = \sup_{0<t<T} \|f(t,\cdot)\|_{L^2},$$

thus we first need to prove that we have the estimates (4.28) and then, if we have the condition (4.29), we will obtain a solution of equation (1.4).

Let us start with the initial data. If we denote by e_0 the quantity $h_t * n_0(x)$, then by the Young inequalities for convolution we can write

$$\|h_t * n_0\|_{L^2} \le \|h_t\|_{L^1} \|n_0\|_{L^2} = \|n_0\|_{L^2},$$

since $\|h_t\|_{L^1} = 1$ and from this uniform in time estimate we obtain

$$\|h_t * n_0\|_{L^\infty_t(L^2_x)} = \sup_{0<t<T} \|h_t * n_0\|_{L^2} \le \|n_0\|_{L^2} < +\infty. \tag{4.30}$$

For the second term of equation (1.4), let us write

$$B(n,n) = \int_0^t h_{t-s} * \left[\partial_x\Big(\chi * n\mathcal{H}(Sn)\Big)\right](s,x)\,\mathrm{d}s,$$

it is easy to see that the quantity $B(\cdot,\cdot)$ is bilinear and we have

$$\|B(n,\nu)\|_{L^\infty_t(L^2_x)} = \sup_{0<t<T} \left\| \int_0^t h_{t-s} * \left[\partial_x\Big(\chi * n\mathcal{H}(S\nu)\Big)\right](s,\cdot)\,\mathrm{d}s \right\|_{L^2},$$

and by the Young inequalities for convolution we can write

$$\begin{aligned}
\|B(n,\nu)\|_{L^\infty_t(L^2_x)} &\le \sup_{0<t<T} \int_0^t \left\| \partial_x h_{t-s} * \Big(\chi * n\mathcal{H}(S\nu)\Big)(s,\cdot) \right\|_{L^2} \mathrm{d}s \\
&\le \sup_{0<t<T} \int_0^t \|\partial_x h_{t-s}\|_{L^2} \|\chi * n\mathcal{H}(S\nu)(s,\cdot)\|_{L^1}\,\mathrm{d}s,
\end{aligned}$$

since by (3.26) we have $\|\partial_x h_{t-s}\|_{L^2} \le C(t-s)^{-\frac{3}{4}}$, by the Hölder and Young inequalities we can write

$$\begin{aligned}
\|B(n,\nu)\|_{L^\infty_t(L^2_x)} &\le C \sup_{0<t<T} \int_0^t (t-s)^{-\frac{3}{4}} \|\chi(s,\cdot)\|_{L^1} \|n(s,\cdot)\|_{L^2} \|\mathcal{H}(S\nu)(s,\cdot)\|_{L^2}\,\mathrm{d}s \\
&\le C \sup_{0<t<T} \int_0^t (t-s)^{-\frac{3}{4}} \|\chi(s,\cdot)\|_{L^1} \|n(s,\cdot)\|_{L^2} \|(S\nu)(s,\cdot)\|_{L^2}\,\mathrm{d}s,
\end{aligned}$$

where in the last estimate we used the fact that the Hilbert transform $\mathcal{H}$ is a bounded operator in the Lebesgue space $L^2(\mathbb{R})$. Next we write

$$\begin{aligned}
&\|B(n,\nu)\|_{L^\infty_t(L^2_x)} \\
\le\;& C\|\chi\|_{L^\infty_t(L^1_x)} \|n\|_{L^\infty_t(L^2_x)} \|S\|_{L^\infty_t(L^\infty_x)} \|\nu\|_{L^\infty_t(L^2_x)} \sup_{0<t<T} \int_0^t (t-s)^{-\frac{3}{4}}\,\mathrm{d}s \\
\le\;& CT^{\frac{1}{4}} \|\chi\|_{L^\infty_t(L^1_x)} \|S\|_{L^\infty_t(L^\infty_x)} \|n\|_{L^\infty_t(L^2_x)} \|\nu\|_{L^\infty_t(L^2_x)}. \qquad (4.31)
\end{aligned}$$

Now, with the estimates (4.30) and (4.31) if the following condition is satisfied

$$\|n_0\|_{L^2} < \frac{1}{4CT^{\frac{1}{4}}\|\chi\|_{L^\infty_t(L^1_x)}\|S\|_{L^\infty_t(L^\infty_x)}},$$

we obtain a unique solution of the equation (1.10). Thus, as long as we have

$$T < \frac{1}{\left(C\|n_0\|_{L^2}\|\chi\|_{L^\infty_t(L^1_x)}\|S\|_{L^\infty_t(L^\infty_x)}\right)^4}, \tag{4.32}$$

we have the existence and the uniqueness of the solution of this problem.

4.2 Proof of Theorem 2

Here, we study the existence of local solutions for the trilinear system (4.34). For the sake of completeness we state and proof a variant of the Banach-Picard fixed point theorem which will give us a suitable framework in order to study a trilinear problem.

Theorem 6 (Trilinear Banach-Picard fixed point). *Let $(E, \|\cdot\|_E)$ be a Banach space et consider $B : E \times E \times E \longrightarrow E$ a bounded trilinear application:*

$$\|B(e, f, g)\|_E \leq C_B\|e\|_E\|f\|_E\|g\|_E. \tag{4.33}$$

If $e_0 \in E$ is such that $\|e_0\|_E \leq \delta$ and if $0 < \delta^2 < \frac{1}{12C_B}$, then the equation

$$e = e_0 + B(e, e, e), \tag{4.34}$$

admits a unique solution $e \in E$ such that $\|e\|_E \leq 2\delta$.

Proof. From the initial data e_0 we write

$$e_{n+1} = e_0 + B(e_n, e_n, e_n),$$

and let us prove that $\|e_{n+1}\|_E \leq 2\delta$. This is true for e_0 and assume that $\|e_n\|_E \leq 2\delta$, thus by the boundedness of $B(\cdot, \cdot, \cdot)$ given in (4.33) we have

$$\|e_{n+1}\|_E \leq \|e_0\|_E + \|B(e_n, e_n, e_n)\|_E \leq \|e_0\|_E + C_B\|e_n\|_E^3 \leq \delta + 8C_B\delta^3,$$

but since we have $8C_B\delta^2 < 12C_B\delta^2 < 1$, we can write

$$\|e_{n+1}\|_E \leq \delta + 8C_B\delta^3 = \delta + (8C_B\delta^2)\delta \leq 2\delta,$$

and we have proven that for all $n \geq 1$, the element e_n belongs to $\overline{B}(0, 2\delta)$.

We will prove now that we can obtain a solution e when $n \to +\infty$ and we study $e_{n+1} - e_n$ and using the trilinearity of the application $B(\cdot, \cdot, \cdot)$ we have:

$$\begin{aligned}
\|e_{n+1} - e_n\|_E &= \|(e_0 + B(e_n, e_n, e_n)) - (e_0 + B(e_{n-1}, e_{n-1}, e_{n-1}))\|_E \\
&= \|B(e_n, e_n, e_n) - B(e_{n-1}, e_{n-1}, e_{n-1})\|_E \\
&= \|B(e_n - e_{n-1}, e_n, e_n) + B(e_{n-1}, e_n - e_{n-1}, e_{n-1}) \\
&\quad + B(e_{n-1}, e_n, e_n - e_{n-1})\|_E \\
&\leq \|B(e_n - e_{n-1}, e_n, e_n)\|_E + \|B(e_{n-1}, e_n - e_{n-1}, e_{n-1})\|_E \\
&\quad + \|B(e_{n-1}, e_n, e_n - e_{n-1})\|_E,
\end{aligned}$$

using now the boundedness of the application $B(\cdot,\cdot,\cdot,)$ we can write

$$\begin{aligned}\|e_{n+1}-e_n\|_E &\leq C_B\|e_n-e_{n-1}\|_E\|e_n\|_E\|e_n\|_E + C_B\|e_{n-1}\|_E\|e_n-e_{n-1}\|_E\|e_{n-1}\|_E\\ &\quad +C_n\|e_{n-1}\|_E\|e_n\|_E\|e_n-e_{n-1}\|_E,\end{aligned}$$

and since we have $\|e_{n-1}\|_E \leq 2\delta$ and $\|e_n\|_E \leq 2\delta$, we obtain

$$\|e_{n+1}-e_n\|_E \leq 12C_B\delta^2\|e_n-e_{n-1}\|_E,$$

thus, by iteration we have

$$\|e_{n+1}-e_n\|_E \leq \left(12C_B\delta^2\right)^n\|e_1-e_0\|_E,$$

but since $12C_B\delta^2 < 1$, we have

$$\lim_{n\to+\infty}\|e_{n+1}-e_n\|_E = 0,$$

and thus the sequence $(e_n)_{n\in\mathbb{N}}$ converges to a point e in E which satisfies the equation (4.34). Unicity is granted as we are working in a Banach space. □

In order to apply the previous theorem to the system (1.2) we use the vectorial quantities $\vec{\theta}_0(x), \vec{\theta}(t,x)$ and $\vec{\mathbb{S}}_{[\vec{\theta}]}(t,x)$ defined by (1.5) and (1.6). Recall that if $\vec{a}(t,x) = \begin{bmatrix} a_1(t,x)\\ a_2(t,x)\end{bmatrix}$ is a vector, then we will say that $\vec{a}\in L^\infty_t(L^2_x)$ if

$$\|\vec{a}\|_{L^\infty_t(L^2_x)} = \big\|(|a_1|+|a_2|)\big\|_{L^\infty_t(L^2_x)} < +\infty.$$

Note in particular that we always have the estimate $\|a_j\|_{L^\infty_t(L^2_x)} \leq \|\vec{a}\|_{L^\infty_t(L^2_x)}$ for all $j=1,2$.

In order to apply Theorem 6 to the previous problem, we will consider its integral representation (Duhamel's formula) given by (1.8):

$$\vec{\theta}(t,x) = h_t * \vec{\theta}_0(x) + \int_0^t h_{t-s} * \partial_x\vec{\mathbb{S}}_{[\vec{\theta}]}(s,x)\,\mathrm{d}s.$$

At this point, we remark that due to the definition of the terms S_1 and S_2 given in (1.3) we actually have

$$\vec{\mathbb{S}}_{[\vec{\theta}]} = \begin{bmatrix}\chi_1 * n_1\mathcal{H}(S_2n_1)\\ \chi_2 * n_2\mathcal{H}(S_1n_2)\end{bmatrix} = \begin{bmatrix}\chi_1 * n_1\mathcal{H}\big((K_2*n_2)n_1\big)\\ \chi_2 * n_2\mathcal{H}\big((K_1*n_1)n_2\big)\end{bmatrix},$$

which is of the form:

$$\begin{bmatrix}\chi_1 * e_1\mathcal{H}\big((K_2*f_2)g_1\big)\\ \chi_2 * e_2\mathcal{H}\big((K_1*f_1)g_2\big)\end{bmatrix} = B\big(\vec{e},\vec{f},\vec{g}\big),$$

where the quantity $B(\cdot,\cdot,\cdot)$ is trilinear and thus the whole integral in (1.8) is itself a trilinear application, thus this equation is of the form (4.34) and we are in the setting of the Theorem 6.

Proof of Theorem 2. Following Theorem 6, we will first prove the estimates

- for the initial data:
$$\|h_t * \vec{\theta}_0\|_{L^\infty_t(L^2_x)} \leq \|\vec{\theta}_0\|_{L^2},$$
- for the trilinear term:
$$\left\|\int_0^t h_{t-s} * \partial_x\vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)} \leq C_B\|\vec{\theta}\|^3_{L^\infty_t(L^2_x)},$$

  where C_B way depend on the kernels K_1, K_2 and on the time variable.

Indeed, for the initial data we readily have

$$\|h_t * \vec{\theta}_0\|_{L^\infty_t(L^2_x)} \leq \|h_t\|_{L^1}\|\vec{\theta}_0\|_{L^2} = \|\vec{\theta}_0\|_{L^2}.$$

For the trilinear term we write

$$\begin{aligned}\left\|\int_0^t h_{t-s} * \partial_x \vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)} &= \sup_{0<t<T}\left\|\int_0^t \partial_x h_{t-s} * \vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s\right\|_{L^2}\\ &\leq \sup_{0<t<T}\int_0^t \|\partial_x h_{t-s}\|_{L^2}\|\vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\|_{L^1}\,\mathrm{d}s,\end{aligned}$$

and since $\|\partial_x h_{t-s}\|_{L^2} \leq C(t-s)^{-\frac{3}{4}}$ by (3.26), we have

$$\begin{aligned}&\left\|\int_0^t h_{t-s} * \partial_x \vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)}\\ \leq\ & C\sup_{0<t<T}\int_0^t (t-s)^{-\frac{3}{4}}\Big(\|\chi_1 * n_1\mathcal{H}\big((K_2 * n_2)n_1\big)(s,\cdot)\|_{L^1}\\ &\qquad +\|\chi_2 * n_2\mathcal{H}\big((K_1 * n_1)n_2\big)(s,\cdot)\|_{L^1}\Big)\,\mathrm{d}s.\end{aligned}$$

Next, by the Hölder and the Young inequalities it comes:

$$\begin{aligned}&\left\|\int_0^t h_{t-s} * \partial_x \vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)}\\ \leq\ & C\sup_{0<t<T}\int_0^t (t-s)^{-\frac{3}{4}}\Big(\|\chi_1(s,\cdot)\|_{L^1}\|n_1(s,\cdot)\|_{L^2}\|\mathcal{H}\big((K_2 * n_2)n_1\big)(s,\cdot)\|_{L^2}\\ &\qquad +\|\chi_2(s,\cdot)\|_{L^1}\|n_2(s,\cdot)\|_{L^2}\|\mathcal{H}\big((K_1 * n_1)n_2\big)(s,\cdot)\|_{L^2}\Big)\,\mathrm{d}s,\end{aligned}$$

we use now the boundedness of the Hilbert transform $\mathcal{H}$ in the Lebesgue spaces L^2 to write

$$\begin{aligned}&\left\|\int_0^t h_{t-s} * \partial_x \vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)}\\ \leq\ & C\sup_{0<t<T}\int_0^t (t-s)^{-\frac{3}{4}}\Big(\|\chi_1(s,\cdot)\|_{L^1}\|n_1(s,\cdot)\|_{L^2}\|(K_2 * n_2)n_1(s,\cdot)\|_{L^2}\\ &\qquad +\|\chi_2(s,\cdot)\|_{L^1}\|n_2(s,\cdot)\|_{L^2}\|(K_1 * n_1)n_2(s,\cdot)\|_{L^2}\Big)\,\mathrm{d}s\\ \leq\ & C\sup_{0<t<T}\int_0^t (t-s)^{-\frac{3}{4}}\Big(\|\chi_1(s,\cdot)\|_{L^1}\|n_1(s,\cdot)\|_{L^2}\|K_2 * n_2(s,\cdot)\|_{L^\infty}\|n_1(s,\cdot)\|_{L^2}\\ &\qquad +\|\chi_2(s,\cdot)\|_{L^1}\|n_2(s,\cdot)\|_{L^2}\|K_1 * n_1(s,\cdot)\|_{L^\infty}\|n_2(s,\cdot)\|_{L^2}\Big)\,\mathrm{d}s.\end{aligned}$$

Applying the Young inequalities in the convolutions above we obtain

$$\begin{aligned}
&\left\| \int_0^t h_{t-s} * \partial_x \vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s \right\|_{L_t^\infty(L_x^2)} \\
\leq\ & C \sup_{0<t<T} \int_0^t (t-s)^{-\frac{3}{4}} \Big(\|\chi_1(s,\cdot)\|_{L^1} \|n_1(s,\cdot)\|_{L^2} \|K_2\|_{L^2} \|n_2(s,\cdot)\|_{L^2} \|n_1(s,\cdot)\|_{L^2} \\
&\qquad + \|\chi_2(s,\cdot)\|_{L^1} \|n_2(s,\cdot)\|_{L^2} \|K_1\|_{L^2} \|n_1(s,\cdot)\|_{L^2} \|n_2(s,\cdot)\|_{L^2} \Big)\,\mathrm{d}s \\
\leq\ & C \Big(\|\chi_1\|_{L_t^\infty(L_x^1)} \|n_1\|^2_{L_t^\infty(L_x^2)} \|n_2\|_{L_t^\infty(L_x^2)} \|K_2\|_{L^2} \\
&\qquad + \|\chi_2\|_{L_t^\infty(L_x^1)} \|n_2\|^2_{L_t^\infty(L_x^2)} \|n_1\|_{L_t^\infty(L_x^2)} \|K_1\|_{L^2} \Big) \\
&\times \sup_{0<t<T} \int_0^t (t-s)^{-\frac{3}{4}}\,\mathrm{d}s.
\end{aligned}$$

Moreover, since $\|n_1\|_{L_t^\infty(L_x^2)} \leq \|\vec{\theta}\|_{L_t^\infty(L_x^2)}$ and $\|n_2\|_{L_t^\infty(L_x^2)} \leq \|\vec{\theta}\|_{L_t^\infty(L_x^2)}$, we finally have

$$\begin{aligned}
&\left\| \int_0^t h_{t-s} * \partial_x \vec{\mathbb{S}}_{[\vec{\theta}]}(s,\cdot)\,\mathrm{d}s \right\|_{L_t^\infty(L_x^2)} \\
\leq\ & C T^{\frac{1}{4}} \left(\|\chi_1\|_{L_t^\infty(L_x^1)} \|K_1\|_{L^2} + \|\chi_2\|_{L_t^\infty(L_x^1)} \|K_2\|_{L^2} \right) \|\vec{\theta}\|^3_{L_t^\infty(L_x^2)},
\end{aligned}$$

where, as announced $C_B = CT^{\frac{1}{4}}(\|\chi_1\|_{L_t^\infty(L_x^1)} \|K_1\|_{L^2} + \|\chi_2\|_{L_t^\infty(L_x^1)} \|K_2\|_{L^2})$.

Thus, to conclude, we only need to impose the condition

$$\|\vec{\theta}_0\|^2_{L^2} < \frac{1}{12CT^{\frac{1}{4}}(\|\chi_1\|_{L_t^\infty(L_x^1)} \|K_1\|_{L^2} + \|\chi_2\|_{L_t^\infty(L_x^1)} \|K_2\|_{L^2})},$$

which can be rewritten as

$$T < \frac{1}{\left(C\|\vec{\theta}_0\|^2_{L^2} \left(\|\chi_1\|_{L_t^\infty(L_x^1)} \|K_1\|_{L^2} + \|\chi_2\|_{L_t^\infty(L_x^1)} \|K_2\|_{L^2} \right) \right)^4}, \tag{4.35}$$

and this achieves the proof. $\square$

Remark 4.1. *It is worth noting here that the conditions (4.32) and (4.35) allow us to consider large initial data (n_0 or $\vec{\theta}_0$), large functions χ_i and large kernels (S_i or K_i) in the L^2-sense. The price to pay is a corresponding potentially very small time of existence.*

Remark 4.2. *Other (and much more general) functional spaces can be considered here such as Morrey spaces or Besov/Triebel-Lizorkin spaces and we do not claim any optimality of our results.*

The method displayed to prove Theorems 1 and 2 can not treat the case of simultaneous large data and large times of existence, and without an *a priori* information on the $L_t^\infty(L_x^2)$ norm it seems hard to extend in time these local solutions. However, if we change the framework and we assume some smallness condition on the data, then it is possible to obtain global results as it is explained in the next section.

5 Global Solutions

We study now global in time solutions for the previous equations (1.1) and (1.2). To do so, we will consider a slightly different approach. Indeed, although we are still looking for mild solutions via a Banach-Picard fixed point algorithm, the space $L_t^\infty(L_x^2)$ does not seem well suited for this purpose. Instead, we will consider a smaller functional space $E = L_t^\infty(L_x^2) \cap L_t^2(\dot{H}_x^1)$ which captures more regularity information. This space $L_t^\infty(L_x^2) \cap L_t^2(\dot{H}_x^1)$ can be endowed with the norm

$$\|f\|_E = \|\cdot\|_{L_t^\infty(L_x^2)} + \|\cdot\|_{L_t^2(\dot{H}_x^1)} = \sup_{t>0} \|f(t,\cdot)\|_{L^2} + \left(\int_0^{+\infty} \|f(t,\cdot)\|_{\dot{H}^1}^2 \,\mathrm{d}t\right)^{\frac{1}{2}}. \tag{5.36}$$

In the next section, we first gather some classical inequalities on the norms $\|\cdot\|_E$, $\|\cdot\|_{L_t^\infty(L_x^2)}$ and $\|\cdot\|_{L_t^2(\dot{H}_x^1)}$.

5.1 Useful estimates

Lemma 5.1. *If $f \in L^2(\mathbb{R})$ then $h_t * f \in L^2([0,+\infty[, \dot{H}^1(\mathbb{R}))$ and we have*

$$\|h_t * f\|_{L_t^2(\dot{H}_x^1)} \leq C\|f\|_{L^2}.$$

Proof. By the Plancherel formula and the Fubini theorem, we have

$$\|h_t * f\|_{L_t^2(\dot{H}_x^1)}^2 \simeq \int_0^{+\infty} \int_{\mathbb{R}} |\xi|^2 e^{-2t|\xi|^2} |\widehat{f}(\xi)|^2 \,\mathrm{d}\xi \,\mathrm{d}t = \int_{\mathbb{R}} \int_0^{+\infty} |\xi|^2 e^{-2t|\xi|^2} |\widehat{f}(\xi)|^2 \,\mathrm{d}t \,\mathrm{d}\xi.$$

Set $\tau = 2t|\xi|^2$, then

$$\|h_t * f\|_{L_t^2(\dot{H}_x^1)}^2 \simeq \frac{1}{2} \int_{\mathbb{R}} \int_0^{+\infty} e^{-\tau} |\widehat{f}(\xi)|^2 \,\mathrm{d}\tau \,\mathrm{d}\xi = \frac{1}{2}\|\widehat{f}\|_{L^2}^2,$$

from which the result follows. □

Define

$$F(t,x) = \int_0^t h_{t-s} * f(s,x) \,\mathrm{d}s.$$

Lemma 5.2. *If $f \in L^2([0,+\infty[, L^2(\mathbb{R}^3))$, then we have*

$$\|\partial_{xx} F(\cdot,\cdot)\|_{L_t^2(L_x^2)} \leq C\|f\|_{L_t^2(L_x^2)}.$$

This estimate is known as the maximal regularity of the heat kernel.

Proof. A general proof can be found in [11], but we give here the details for the sake of completeness. Since we have

$$\partial_{xx} F(t,x) = \int_0^t \partial_{xx}[h_{t-s}] * f(s,x) \,\mathrm{d}s,$$

taking the Fourier transform in the space variable, with a change of variables in the time variable, it comes

$$\begin{aligned} \mathcal{F}_x\left[\partial_{xx}F\right](t,\xi) &= \int_0^t -|\xi|^2 e^{-(t-s)|\xi|^2} \mathcal{F}_x\left[f\right](s,\xi) \,\mathrm{d} \\ &= \int_0^t -|\xi|^2 e^{-\eta|\xi|^2} \mathcal{F}_x\left[f\right](t-\eta,\xi) \,\mathrm{d}\eta. \end{aligned}$$

Setting $f(t,x)=0$ if $t<0$, we obtain

$$\mathcal{F}_x\left[\partial_{xx}F\right](t,\xi)=\int_0^{+\infty}-|\xi|^2e^{-\eta|\xi|^2}\mathcal{F}_x\left[f\right](t-\eta,\xi)\,\mathrm{d}\eta,$$

taking now the Fourier transform in the time variable and by the Fubini theorem, we have

$$\begin{aligned}
\mathcal{F}_{t,x}\left[\partial_{xx}F\right](\tau,\xi) &= \int_{-\infty}^{+\infty}\left(\int_0^{+\infty}-|\xi|^2e^{-\eta|\xi|^2}\mathcal{F}_x\left[f\right](t-\eta,\xi)\,\mathrm{d}\eta\right)e^{-it\tau}\,\mathrm{d}t\\
&= \int_0^{+\infty}-|\xi|^2e^{-\eta|\xi|^2}\left(\int_{-\infty}^{+\infty}\mathcal{F}_x\left[f\right](t-\eta,\xi)e^{-it\tau}\,\mathrm{d}t\right)\mathrm{d}\eta\\
&= \int_0^{+\infty}-|\xi|^2e^{-\eta|\xi|^2}\left(e^{-i\eta\tau}\mathcal{F}_{t,x}\left[f\right](\tau,\xi)\right)\mathrm{d}\eta\\
&= \frac{-|\xi|^2}{|\xi|^2+i\tau}\mathcal{F}_{t,x}\left[f\right](\tau,\xi).
\end{aligned}$$

We remark now that the symbol $\frac{-|\xi|^2}{|\xi|^2+i\tau}$ is bounded, and thus we can write

$$\|\partial_{xx}F\|_{L^2_t(L^2_x)}\simeq\|\mathcal{F}_{t,x}\left[\partial_{xx}F\right]\|_{L^2_t(L^2_x)}=\left\|\frac{-|\xi|^2}{|\xi|^2+i\tau}\mathcal{F}_{t,x}\left[f\right]\right\|_{L^2_t(L^2_x)}\leq C\|f\|_{L^2_t(L^2_x)},$$

which achieves the proof of the lemma. □

Our last result concerns the norm $\|\cdot\|_E$ defined in (5.36).

Proposition 5.1. *If $f\in L^2\big([0,+\infty[,\dot H^{-1}(\mathbb{R})\big)$ then we have the following estimate for the norm $\|\cdot\|_E$ given by (5.36):*

$$\left\|\int_0^t h_{t-s}*f(s,\cdot)\,\mathrm{d}s\right\|_E\leq C\|f\|_{L^2_t(\dot H^{-1}_x)}.$$

Proof. By definition of the norm $\|\cdot\|_E$ we have

$$\begin{aligned}
\left\|\int_0^t h_{t-s}*f(s,\cdot)\,\mathrm{d}s\right\|_E &= \underbrace{\left\|\int_0^t h_{t-s}*f(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)}}_{(a)}\\
&\quad+\underbrace{\left\|\int_0^t h_{t-s}*f(s,\cdot)\,\mathrm{d}s\right\|_{L^2_t(\dot H^1_x)}}_{(b)}.
\end{aligned}\tag{5.37}$$

We start by the term (a) and we write

$$\left\|\int_0^t h_{t-s}*f(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)}=\sup_{0\leq t\leq T}\left\|\int_0^t h_{t-s}*f(s,\cdot)\,\mathrm{d}s\right\|_{L^2}.$$

By the L^2-L^2 duality we obtain

$$\begin{aligned}
\left\|\int_0^t h_{t-s}*f(s,\cdot)\,\mathrm{d}s\right\|_{L^2} &= \sup_{\|\phi\|_{L^2}\leq1}\left|\int_{\mathbb{R}}\left(\int_0^t h_{t-s}*f(s,x)\,\mathrm{d}s\right)\phi(x)\,\mathrm{d}x\right|\\
&= \sup_{\|\phi\|_{L^2}\leq1}\left|\int_{\mathbb{R}}\int_0^t\int_{\mathbb{R}}h_{t-s}(x-y)f(s,y)\phi(x)\,\mathrm{d}y\,\mathrm{d}s\,\mathrm{d}x\right|\\
&= \sup_{\|\phi\|_{L^2}\leq1}\left|\int_0^t\int_{\mathbb{R}}h_{t-s}*\phi(y)f(s,y)\,\mathrm{d}y\,\mathrm{d}s\right|.
\end{aligned}$$

Now, using the $\dot{H}^1 - \dot{H}^{-1}$ duality we can write

$$\begin{aligned}\left\|\int_0^t h_{t-s} * f(s,\cdot)\,\mathrm{d}s\right\|_{L^2} &\leq \sup_{\|\phi\|_{L^2}\leq 1}\left(\int_0^t \|h_{t-s}*\phi\|_{\dot{H}^1}\|f(s,\cdot)\|_{\dot{H}^{-1}}\,\mathrm{d}s\right)\\ &\leq \|f\|_{L^2_t(\dot{H}^{-1}_x)}\sup_{\|\phi\|_{L^2}\leq 1}\|h_{t-s}*\phi\|_{L^2_t(\dot{H}^1_x)},\end{aligned}$$

where we used the Cauchy-Schwarz inequality in the time variable. Now using Lemma 5.1, we have $\|h_{t-s}*\phi\|_{L^2_t(\dot{H}^1_x)} \leq \|\phi\|_{L^2}$, hence, we obtain

$$\left\|\int_0^t h_{t-s} * f(s,\cdot)ds\right\|_{L^2} \leq C\|f\|_{L^2_t(\dot{H}^{-1}_x)}\sup_{\|\phi\|_{L^2}\leq 1}\|\phi\|_{L^2} \leq C\|f\|_{L^2_t(\dot{H}^{-1}_x)},$$

and from this uniform estimate in the time variable it follows

$$\left\|\int_0^t h_{t-s} * f(s,\cdot)\,\mathrm{d}s\right\|_{L^\infty_t(L^2_x)} \leq C\|f\|_{L^2_t(\dot{H}^{-1}_x)}. \tag{5.38}$$

We study now (b) and we write:

$$\begin{aligned}\left\|\int_0^t h_{t-s} * f(s,\cdot)\,\mathrm{d}s\right\|_{L^2_t(\dot{H}^1_x)} &= \left\|\int_0^t h_{t-s} * (-\Delta_x)^{\frac{1}{2}} f(s,\cdot)\,\mathrm{d}s\right\|_{L^2_t(L^2_x)}\\ &= \left\|\int_0^t h_{t-s} * \partial_{xx}\left[(-\Delta_x)^{-\frac{1}{2}} f(s,\cdot)\right]\,\mathrm{d}s\right\|_{L^2_t(L^2_x)}\\ &= \left\|\partial_{xx}\int_0^t h_{t-s} * \left[(-\Delta_x)^{-\frac{1}{2}} f(s,\cdot)\right]\,\mathrm{d}s\right\|_{L^2_t(L^2_x)},\end{aligned}$$

where $(-\Delta_x)^{\frac{1}{2}}$ is the one dimensional operator of symbol $|\xi|$. We apply now the maximal regularity of the heat kernel given in Lemma 5.2 to obtain

$$\left\|\partial_{xx}\int_0^t h_{t-s} * \left[(-\Delta_x)^{-\frac{1}{2}} f(s,\cdot)\right]\,\mathrm{d}s\right\|_{L^2_t(L^2_x)} \leq C\left\|(-\Delta_x)^{-\frac{1}{2}} f\right\|_{L^2_t(L^2_x)},$$

and we thus have

$$\left\|\int_0^t h_{t-s} * f(s,\cdot)\,\mathrm{d}s\right\|_{L^2_t(\dot{H}^1_x)} \leq C\|f\|_{L^2_t(\dot{H}^{-1}_x)}. \tag{5.39}$$

With estimates (5.38) – (5.39) and coming back to (5.37) we finally obtain:

$$\left\|\int_0^t h_{t-s} * f(s,\cdot)\,\mathrm{d}s\right\|_E \leq C\|f\|_{L^2_t(\dot{H}^{-1}_x)},$$

which ends the proof of the proposition. □

5.2 Proof of Theorem 3.

With the results established in the previous sections, we can study the global existence for the bilinear system (1.1). Considering the formulation (1.10) above, we will apply the same arguments as in Theorem 1 (*i.e.* a fixed point argument) but using the functional space $E = L^\infty([0,+\infty], L^2(\mathbb{R})) \cap L^2([0,+\infty], \dot{H}^1(\mathbb{R}))$ endowed with the norm $\|\cdot\|_E$ given in (5.36). Thus, we have to prove the estimates (4.28) and (4.29) to obtain a solution. If the constants involved in these estimates do not depend on the time variable, we will obtain global solutions in time.

Setting $e_0 = h_t * n_0(x)$ and $B(n,n) = \displaystyle\int_0^t h_{t-s} * \left[\partial_x\Big(\chi * n\mathcal{H}(Sn)\Big)\right](s,x)\,\mathrm{d}s$, we need to prove:

$$\|e_0\|_E \leq \delta \qquad \text{and} \qquad \|B(n,n)\|_E \leq C_B\|n\|_E\|n\|_E. \tag{5.40}$$

Moreover, if we have the condition

$$\delta < \frac{1}{4C_B}, \tag{5.41}$$

then we obtain a unique solution of the problem (1.10) in the functional space E.

Let us start with the first estimate of (5.40). First, if $n_0 \in L^2(\mathbb{R})$, we get

$$\|h_t * n_0\|_{L^2} \leq \|h_t\|_{L^1}\|n_0\|_{L^2} = \|n_0\|_{L^2}.$$

Moreover, by Lemma 5.1 we have $\|h_t * n_0\|_{L^2_t(\dot{H}^1_x)} \leq C\|n_0\|_{L^2}$ and we can thus write

$$\|h_t * n_0\|_E \leq C_1\|n_0\|_{L^2}. \tag{5.42}$$

We study now the second estimate of (5.40) which is given by the quantity

$$\|B(n,n)\|_E = \left\|\int_0^t h_{t-s} * \partial_x\big(\chi * n\mathcal{H}(Sn)\big)(s,x)\,\mathrm{d}s\right\|_E.$$

Applying Proposition 5.1 we have

$$\begin{aligned}\left\|\int_0^t h_{t-s} * \partial_x\big(\chi * n\mathcal{H}(Sn)\big)(s,x)\,\mathrm{d}s\right\|_E &\leq C\left\|\partial_x\big(\chi * n\mathcal{H}(Sn)\big)\right\|_{L^2_t(\dot{H}^{-1}_x)}\\ &= C\|\chi * n\mathcal{H}(Sn)\|_{L^2_t(L^2_x)}.\end{aligned}$$

Let us study the last quantity above in the space variable. We first see that

$$\|\chi * n\mathcal{H}(Sn)(t,\cdot)\|_{L^2} \leq \|\chi(t,\cdot)\|_{L^2}\|n(t,\cdot)\mathcal{H}(Sn)(t,\cdot)\|_{L^1} \leq \|\chi(t,\cdot)\|_{L^2}\|n(t,\cdot)\|_{L^2}\|\mathcal{H}(Sn)(t,\cdot)\|_{L^2},$$

hence, by the boundedness of the Hilbert transform in Lebesgue spaces together with the hypothesis $S(t,\cdot) \in L^\infty(\mathbb{R})$, we have

$$\|\chi * n\mathcal{H}(Sn)(t,\cdot)\|_{L^2} \leq C\|\chi(t,\cdot)\|_{L^2}\|n(t,\cdot)\|_{L^2}\|S(t,\cdot)\|_{L^\infty}\|n(t,\cdot)\|_{L^2}.$$

Taking the L^2-norm in the time variable it yields

$$\|\chi * n\mathcal{H}(Sn)\|_{L^2_t(L^2_x)} \leq C_2\|\chi\|_{L^2_t(L^2_x)}\|S\|_{L^\infty_t(L^\infty_x)}\|n\|_{L^\infty_t(L^2_x)}\|n\|_{L^\infty_t(L^2_x)}.$$

Consequently, reconstructing the norm $\|\cdot\|_E$ given in (5.36), we get the estimate

$$\left\|\int_0^t h_{t-s} * \partial_x\big(\chi * n\mathcal{H}(Sn)\big)(s,x))\,\mathrm{d}s\right\|_E \leq C_B\|n\|_E\|n\|_E, \tag{5.43}$$

where $C_B = C_2\|\chi\|_{L^2_t(L^2_x)}\|S\|_{L^\infty_t(L^\infty_x)}$. Now, from (5.42) and (5.43) if we have

$$C_1\|n_0\|_{L^2} < \frac{1}{4C_2\|\chi\|_{L^2_t(L^2_x)}\|S\|_{L^\infty_t(L^\infty_x)}},$$

then the condition (5.41) is fulfilled (by choosing carefully the constant $\mathfrak{C}$ given in (1.9)) and we can apply a fixed point argument to obtain a unique global solution since the time variable does not intervene in the estimates.

5.3 Proof of Theorem 4.

Here, we study global Solutions for the trilinear system (1.2). Following the idea given in formula (1.8) above, we introduce the term

$$\vec{\mathbb{S}}^*_{[\vec{\theta}]}(t,x) = \begin{bmatrix} \chi_1 * n_1 \mathcal{H}(S_2 n_1) \\ \chi_2 * n_2 \mathcal{H}(S_1 n_2) \end{bmatrix} (t,x),$$

and with the variable $\vec{\theta}$ defined in (1.5) the system (1.2) can be rewritten as

$$\vec{\theta}(t,x) = h_t * \vec{\theta}_0(x) + \int_0^t h_{t-s} * \partial_x \vec{\mathbb{S}}^*_{[\vec{\theta}]}(s,x))\, \mathrm{d}s \tag{5.44}$$

We are going to apply Theorem 6 in the functional space $E = L^\infty([0,+\infty], L^2(\mathbb{R})) \cap L^2([0,+\infty], \dot{H}^1(\mathbb{R}))$ and for this we need to establish the required inequalities.

For the initial data satisfying the estimate (5.42) we have

$$\|h_t * \vec{\theta}_0\|_{L^\infty_t(L^2_x)} \leq \|\vec{\theta}_0\|_{L^2} \qquad \text{and} \qquad \|h_t * \vec{\theta}_0\|_{L^2_t(\dot{H}^1_x)} \leq C\|\vec{\theta}_0\|_{L^2},$$

hence

$$\|h_t * \vec{\theta}_0\|_E \leq C_1 \|\vec{\theta}_0\|_{L^2}. \tag{5.45}$$

For the trilinear term we need to prove the following estimate

$$\left\| \int_0^t h_{t-s} * \partial_x \mathbb{S}^*_{[\,]}\vec{\theta}(s,\cdot))\, \mathrm{d}s \right\|_E \leq C_B \|\vec{\theta}\|^3_E, \tag{5.46}$$

where C_B may depend on the kernels K_1, K_2. By Proposition 5.1 we know that

$$\left\| \int_0^t h_{t-s} * \partial_x \mathbb{S}^*_{[\,]}\vec{\theta}(s,\cdot))\, \mathrm{d}s \right\|_E \;\leq\; \|\partial_x \mathbb{S}^*_{[\,]}\vec{\theta}\|_{L^2_t(\dot{H}^{-1}_x)} \leq \|\mathbb{S}^*_{[\,]}\vec{\theta}\|_{L^2_t(L^2_x)}.$$

Moreover, by definition, we have

$$\|\mathbb{S}^*_{[\,]}\vec{\theta}\|_{L^2_t(L^2_x)} \leq \|\chi_1 * n_1 \mathcal{H}(S_2 n_1)\|_{L^2_t(L^2_x)} + \|\chi_2 * n_2 \mathcal{H}(S_1 n_2)\|_{L^2_t(L^2_x)}. \tag{5.47}$$

For $1 \leq i,j,k \leq 2$, let us now study the term $\|\chi_i * n_i \mathcal{H}(S_j n_k)(t,\cdot)\|_{L^2}$. By the Young and Hölder inequalities and by the boundedness of the Hilbert transform in Lebesgue spaces, we obtain

$$\begin{aligned} \|\chi_i * n_i \mathcal{H}(S_j n_k)(t,\cdot)\|_{L^2} &\leq \|\chi_i(t,\cdot)\|_{L^2} \|n_i(t,\cdot)\|_{L^2} \|\mathcal{H}(S_j n_k)(t,\cdot)\|_{L^2} \\ &\leq C\|\chi_i(t,\cdot)\|_{L^2} \|n_i(t,\cdot)\|_{L^2} \|S_j(t,\cdot) n_k(t,\cdot)\|_{L^2} \\ &\leq C\|\chi_i(t,\cdot)\|_{L^2} \|n_i(t,\cdot)\|_{L^2} \|(K_j * n_j)(t,\cdot) n_k(t,\cdot)\|_{L^2}, \end{aligned}$$

where in the last line we used the fact that $S_j(t,\cdot) = K_j * n_j(t,\cdot)$. Hence, we have

$$\begin{aligned} \|\chi_i * n_i(t,\cdot)\mathcal{H}(S_j n_k)(t,\cdot)\|_{L^2} &\leq C\|\chi_i(t,\cdot)\|_{L^2} \|n_i(t,\cdot)\|_{L^2} \|K_j * n_j(t,\cdot)\|_{L^\infty} \|n_k(t,\cdot)\|_{L^2} \\ &\leq C\|\chi_i(t,\cdot)\|_{L^2} \|n_i(t,\cdot)\|_{L^2} \|K_j\|_{L^2} \|n_j(t,\cdot)\|_{L^2} \|n_k(t,\cdot)\|_{L^2}, \end{aligned}$$

where we used the Young inequalities in the convolution above. Taking this inequality to the power 2 and integrating in the time variable it comes:

$$\begin{aligned} &\left(\int_0^{+\infty} \|\chi_i * n_i \mathcal{H}(S_j n_k)(t,\cdot)\|^2_{L^2}\, \mathrm{d}t \right)^{\frac{1}{2}} \\ &\leq \; C\|K_j\|_{L^2} \|n_i\|_{L^\infty_t(L^2_x)} \|n_j\|_{L^\infty_t(L^2_x)} \|n_k\|_{L^\infty_t(L^2_x)} \left(\int_0^{+\infty} \|\chi_i(t,\cdot)\|^2_{L^2}\, \mathrm{d}t \right)^{\frac{1}{2}}, \end{aligned}$$

and

$$\begin{aligned}\|\chi_i * n_i \mathcal{H}(S_j n_k)\|_{L^2_t(L^2_x)} &\leq C\|\chi_i\|_{L^2_t(L^2_x)}\|K_j\|_{L^2}\|n_i\|_{L^\infty_t(L^2_x)}\|n_j\|_{L^\infty_t(L^2_x)}\|n_k\|_{L^\infty_t(L^2_x)}\\ &\leq C\|\chi_i\|_{L^2_t(L^2_x)}\|K_j\|_{L^2}\|\theta\|_E\|\theta\|_E\|\theta\|_E,\end{aligned}$$

where we used the definition of the quantity θ and of the norm $\|\cdot\|_E$ given in (5.36).

Thus, coming back to (5.47) we obtain

$$\|\mathbb{S}^{\vec{*}}_{[\ ]}\theta\|_{L^2_t(L^2_x)} \leq C(\|\chi_1\|_{L^2_t(L^2_x)}\|K_1\|_{L^2} + \|\chi_2\|_{L^2_t(L^2_x)}\|K_2\|_{L^2})\|\theta\|_E\|\theta\|_E\|\theta\|_E,$$

which leads us to the wished inequality (5.46).

To conclude, with (5.45) and (5.46) at our disposal, following Theorem 6, if we have the condition

$$\|\vec{\theta}_0\|^2_{L^2} < \frac{1}{12C(\|\chi_1\|_{L^2_t(L^2_x)}\|K_1\|_{L^2} + \|\chi_2\|_{L^2_t(L^2_x)}\|K_2\|_{L^2})},$$

we obtain a unique global solution for the problem (5.44).

6 Conclusion

The present paper considers two models to describe yeast cell polarization. In the first model a single cell in a pheromone field is considered. In the second model a system of two coupled equations is considered to describe the cell-cell communication for yeast cells of opposite types. The models include the pheromone concentration (pheromone secretion and pheromone perception) and also a non-constant and nonlocal mobility coefficient, namely the χ function, which describes the mobility of membrane polarity patch and the cell cycle [13, 14]. We provided conditions under which global existence and uniqueness of solutions occur for these two models. Physiologically, yeast cells mate when encountering a partner at close enough range in rich environments. Here, it was shown that even at close enough range and rich enough environment (large values of $\|K_i\|_{L^2}$) cells may not mate when the mobility is low or when one of the cells is leaving the cycle window during which it can mate. Indeed, in such a case global existence might hold true for the solution of the models studied here and then there will be neither polarization nor dialogue. This is in good agreement with biological observations showing that polarization of mating partners towards each other requires the spatial decoding of pheromone gradients, relies on mobile polarity patches and is only possible during a certain period of the cell cycle [13].

We believe this work is the first step towards modelling and understanding the key parameters invoved during the polarization of mating partners towards each other. This represents an important challenge. Future works would be to extend the results of this paper to find conditions for which blow-up of the solution occurs and then to the case of two-dimensional geometry with free boundary.

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