MATHEMATICAL ANALYSIS OF A MODEL OF MORPHOGENESIS

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Abstract. We consider a simple mathematical model of distribution of morphogens (signaling molecules responsible for the differentiation of cells and the creation of tissue patterns) proposed by Lander, Nie and Wan in 2002. The model consists of a system of two equations: a PDE of parabolic type modeling the distribution of free morphogens with a dynamic boundary condition and an ODE describing the evolution of bound receptors. Three biological processes are taken into account: diffusion, degradation and reversible binding. We prove existence and uniqueness of solutions and its asymptotic behavior.

1. Introduction. From the beginning of the formation of the embryo, many different phenomena transform its cells. Some of these phenomena are local, as growth, but others, as differentiation or shapes of tissues or organs and its organization respond to global phenomena. That differentiation of the cell depends on its position in the embryo. The cell receives the information of its position by measuring the concentration of signaling molecules, named morphogens. Morphogenesis (the creation “genesis” of shapes “morphe”) has been studied from the early 20th century, but only in recent years, growth factors have been identified as morphogens.

Morphogens are synthesized at signaling localized sites and spread into the body creating gradients in its concentration as it appears in the experiments (a constant distribution of morphogens would create an homogeneous differentiation of cells). How the gradients arise is an unclear and controversial question and central issue in Development Biology. Theoretical and experimental scientists consider two main theories to explain the formation of gradients of morphogens: diffusion theory, where morphogens are spread by diffusion through the extracellular matrix and the positional theory (see Kerszberg and Wolpert [4]) which suggests that morphogen propagation depends on the closeness of cell-to-cell positions, and morphogens are propagated along cell membranes and transferred between cells that are in contact.

Once the morphogens arrive to the cell surface they bind to receptors and other kind of molecules. The diffusion theory considers slow degradation of products and reversible binding (see Lander, Nie, Wan [6]) in contrast the positional theory does not consider degradation (see Kerszberg and Wolpert [4]).

Lander, Nie and Wan [6] studied numerically several mathematical models and focused on the Drosophila wing disc. They obtain (by using recent experimental
data) that diffusive mechanisms of morphogen transport may produce gradients of morphogens and show that those mechanisms are much more plausible than the non-diffusive ones. They propose several mathematical models, one of them, the diffusion-reversible binding model with degradation is the model which has been analyzed in the following sections. One of the main novelties of that model arises in the peculiar dynamic boundary condition at \( x = 0 \) (see formula (4)).

Lander, Nie, Vargas and Wan [8] and Lander, Nie and Wan [7] proposed several models of differential equations. The models consider a PDE of parabolic type to describe the evolution of morphogens and a set of ODE’s to model the receptor and the bound-receptor. They study the steady states and the linear stability of them under the action of a source in a region of the domain.

Merkin and Sleeman [14] have studied the system proposed by Lander, Nie and Wan [6] with degradation and without it. They provide an analysis of the models under the assumption of constant concentration of morphogens at the boundary \( x = 0 \) and gradient of morphogens equals to zero at infinity. The authors prove that the case where the bound morphogen complex is not degraded, the free morphogen profile is essentially linear and spreads as a square root law.

Recently Merkin, Needham and Sleeman [13] have considered a mathematical model with diffusion and have included a chemosensitivity term to describe morphogen concentration. They have presented results on the existence and uniqueness of classical solutions and self-similarity. Their numerical simulations have showed periodic pulse solutions.

Lou, Nie and Wan [10] consider a model with two species of morphogens. The system consists of three PDE’s of parabolic type and one ODE. They study the steady states and numerical simulation for the evolution problem.

In this work we consider the case of diffusive transport of morphogens. In Section 2 we describe the mathematical model proposed by Lander, Nie and Wan [6]. Section 3 is devoted to the steady states. In Section 4 we introduce the results concerning existence and uniqueness of solutions. Section 5 presents results on asymptotic behavior of the solution. The paper finishes with section 6 where another model of morphogens introduced by Lander, Nie, Vargas and Wan [8] is analyzed.

2. The mathematical model. Different models of distribution of morphogens have been introduced by several authors in the last decade. We study, in the following sections, a simple mathematical model proposed by Lander, Nie and Wan [6] which is described below. They consider the evolution of Decapentaplegic (Dpp) one of the morphogens present in Drosophila larvae wing disc. The model simplifies the geometry of the wing disc considering a one-dimensional domain \((0, \infty)\). We denote by \( L \) the morphogen Dpp (the ligand), by \( R \) the receptor per unit of extracellular space, by \( LR \) the complex ligand-receptor and their respective concentrations by \([L] \), \([R] \) and \([LR] \). The processes, when the ligand \( L \) binds with a receptor \( R \) to form the complex \( LR \) and the reversal are expressed in the following formula

\[
\frac{k_{on}}{k_{off}} L + R \rightleftharpoons LR,
\]

where \( k_{on} \) and \( k_{off} \) are the binding and dissociation rate constants. We assume that the number of receptors (free and bound) is constant on time, i.e.

\[
[R] = R_{tot} - [LR],
\]

(1)
where \( R_{\text{tot}} \) is the total receptor concentration per unit of extracellular space. Assumption [1] reduces the number of equations simplifying the problem. For large intervals of time, degradation of \([LR]\) has to be considered (see Lander, Nie, Vargas, Wan [8]). As we explain in the previous section we consider linear diffusion of \([L]\) with diffusion constant \(d\). Then, \([L]\) satisfies the following equation:

\[
\frac{\partial}{\partial t}[L] - d \frac{\partial^2}{\partial x^2}[L] = -k_{\text{on}}R_{\text{tot}}[L] + k_{\text{on}}[L][LR] + k_{\text{off}}[LR], \quad x > 0, \ t > 0,
\]

(2)

where

\[
d \sim 10^{-13} M^2 s^{-1}; \quad k_{\text{on}} \cdot R_{\text{tot}} \sim 1 - 10^{-2} s^{-1};
\]

\[
k_{\text{on}} \sim 10^5 M^{-1} s^{-1}; \quad k_{\text{off}} \sim 10^{-6} - 10^{-8} s^{-1}
\]

(see Lander, Nie and Wan [6] and references there).

Receptors are fixed in the cells, therefore the equation governing the bound receptor dynamics does not include diffusion. The degradation of the complex is introduced in the model. Let \(k_{\text{deg}}\) be the degradation rate constant, then \([LR]\) satisfies the equation:

\[
\frac{\partial}{\partial t}[LR] = k_{\text{on}}R_{\text{tot}}[L] - k_{\text{on}}[L][LR] - k_{\text{off}}[LR] - k_{\text{deg}}[LR], \quad t > 0,
\]

(3)

where

\[
k_{\text{deg}} \sim 3.3 \cdot 10^{-5} s^{-1}.
\]

We consider that the morphogen is synthesized at \(x = 0\) with rate \(k_{\text{syn}}\) and that the concentration of \([L]\) goes to 0 as \(x\) goes to infinity. Then the boundary conditions for \([L]\) are the following

\[
\frac{\partial}{\partial t}[L] = k_{\text{syn}} - k_{\text{on}}R_{\text{tot}}[L] + k_{\text{on}}[L][LR] + k_{\text{off}}[LR], \quad x = 0, \ t > 0;
\]

\[
\lim_{x \to \infty} [L] = 0, \quad t > 0;
\]

(4)

where

\[
k_{\text{syn}} \sim 5 \cdot 10^{-4}
\]


The system (2)-(4) is completed with the initial data

\[
[L] = [LR] = 0, \quad x > 0, \ t = 0.
\]

(5)

We introduce the dimensionless variables:

\[
\tilde{t} := k_{\text{on}}R_{\text{tot}}t; \quad \tilde{x} := \left(\frac{k_{\text{on}}R_{\text{tot}}}{d}\right)^{1/2} x; \quad u := \frac{k_{\text{on}}}{k_{\text{off}}} [L]; \quad v := \frac{[LR]}{R_{\text{tot}}}
\]

and the parameters

\[
\mu := \frac{k_{\text{deg}}}{k_{\text{off}} R_{\text{tot}}}; \quad \lambda := \frac{k_{\text{off}}}{k_{\text{on}} R_{\text{tot}}}; \quad \nu := \frac{k_{\text{syn}}}{k_{\text{off}} R_{\text{tot}}}
\]

Dropping the tildes and replacing the new variables in equations [2]-[5] we get the dimensionless version of the model:

\[
\frac{\partial u}{\partial \tilde{t}} - \frac{\partial^2}{\partial \tilde{x}^2} u = -u(1 - v) + v, \quad x > 0, \ t > 0,
\]

(6)

\[
\frac{\partial v}{\partial \tilde{t}} = \lambda [u(1 - v) - \mu v], \quad x \geq 0, \ t > 0,
\]

(7)
with boundary conditions
\[
\frac{\partial u}{\partial t} = \nu - u(1 - v) + v, \quad \text{at} \quad x = 0, \quad t > 0, \quad (8)
\]
\[
\lim_{x \to \infty} u(x, t) = 0, \quad t > 0, \quad (9)
\]
and initial data:
\[
u(x, 0) = v(x, 0) = 0, \quad x \geq 0. \quad (10)
\]
Through the paper, we assume for technical reasons in concordance to experimental data that
\[
\frac{\mu}{\lambda} > \nu > 0. \quad (11)
\]
If assumption (11) is not satisfied there do not exist any positive steady states and negative solutions may appear.


Through the following sections we use the notation:
\[
\Omega := (0, \infty); \quad \Omega_T := \Omega \times (0, T).
\]

3. Steady states. We consider the solutions to
\[
0 = \frac{\partial^2}{\partial x^2} \phi - \phi(1 - \xi) + \xi, \quad x > 0, \quad (12)
\]
\[
0 = \lambda [\phi(1 - \xi) - \xi] - \mu \xi, \quad x \geq 0, \quad (13)
\]
satisfying the boundary conditions:
\[
0 = \nu - \phi(1 - \xi) + \xi, \quad \text{at} \quad x = 0, \quad \lim_{x \to \infty} \phi(x) = 0. \quad (14)
\]

**Lemma 1.** For every \(\mu, \lambda, \nu\) satisfying (11) there exists a unique solution \((\phi, \xi)\) to (12)-(14). Moreover, \(\phi\) and \(\xi\) are monotone decreasing functions.

**Proof.** Combining (13) with (14) we get
\[
\xi(0) = \frac{\nu \lambda}{\mu} := \beta < 1,
\]
which, when replaced in (14), yields the boundary condition
\[
\phi(0) = \frac{\nu + \beta}{1 - \beta} = \frac{\nu(\mu + \lambda)}{\mu - \nu \lambda} := \alpha > 0. \quad (15)
\]
Because of (13), \(\xi\) is defined as follows
\[
\xi = \frac{\phi}{\phi + 1 + \tilde{\mu}}, \quad \text{for} \quad \tilde{\mu} := \frac{\mu}{\lambda}.
\]
Hence, (12)-(14) becomes
\[
0 = \frac{\partial^2}{\partial x^2} \phi - \frac{\phi}{\phi + 1 + \tilde{\mu}}, \quad x > 0, \quad (16)
\]
\[
\phi(0) = \alpha.
\]
Multiply equation (16) by \(-{(\phi)}_+\) (where \((\cdot)_+\) is the positive part function) and integrate by parts over \((0, \infty)\) to obtain that \(-{(\phi)}_+ = 0\), i.e \(\phi \geq 0\).

We introduce the system of ODE's

\[
\begin{align*}
\phi' &= \zeta, \\
\zeta' &= \tilde{\mu}\frac{\phi}{\phi + 1 + \tilde{\mu}}.
\end{align*}
\] (17)

We examine the phase portrait of (17) in the half plane \(\phi \geq 0\). The unique equilibrium is \((0, 0)\) and has eigenvalues \(\pm \sqrt{\tilde{\mu}}\), so that \((0, 0)\) is a saddle point.

Notice that:
- \(\phi' > 0, \zeta' > 0\) for \(\phi > 0, \zeta > 0\);
- \(\phi' < 0, \zeta' > 0\) for \(-1 - \tilde{\mu} < \phi < 0, \zeta < 0\);
- \(\phi' > 0, \zeta' < 0\) for \(-1 - \tilde{\mu} < \phi < 0, \zeta > 0\);
- \(\phi' > 0, \zeta' = 0\) for \(\phi = 0, \zeta > 0\);
- \(\phi' = 0, \zeta' > 0\) for \(\phi > 0, \zeta = 0\);
- \(\phi' < 0, \zeta' = 0\) for \(\phi = 0, \zeta < 0\);
- \(\phi' = 0, \zeta' < 0\) for \(-1 - \tilde{\mu} < \phi < 0, \zeta = 0\),

and so there exists a unique orbit which may provide a solution to (17) satisfying

\[
\lim_{x \to \infty} \phi(x) = 0.
\]

We denote by \(\gamma = (\gamma_1, \gamma_2)\) this orbit. To conclude the proof we have to check that \(\gamma\) intersects with \(\phi = \alpha\).

Multiply (17) by \((\phi, \zeta)\) to obtain

\[
\phi\phi' = \zeta\phi,
\]

\[
\frac{1}{2}(\zeta^2)' = \tilde{\mu}\frac{\phi\phi'}{\phi + 1 + \tilde{\mu}},
\]

which implies

\[
\frac{1}{2}(\zeta^2)' = \tilde{\mu}\frac{\phi\phi'}{\phi + 1 + \tilde{\mu}},
\]

and so

\[
\frac{d}{dx} \left( \frac{1}{2} \zeta^2 - \tilde{\mu}\phi - \tilde{\mu} \ln(\phi + 1 + \tilde{\mu}) \right) = 0,
\]

i.e.

\[
\frac{1}{2}\zeta^2(x) - \tilde{\mu}\phi(x) - \tilde{\mu} \ln(\phi(x) + 1 + \tilde{\mu}) = \text{const.}
\] (18)

Since \(\gamma\) belongs to the region \(\phi > 0, \zeta < 0\); there are no periodic orbits and the unique equilibrium is \((0, 0)\) we have that

\[
\lim_{x \to -\infty} |\gamma| = \infty.
\] (19)

(18) and (19) imply that

\[
\lim_{x \to -\infty} \gamma_1 = \infty, \quad \lim_{x \to -\infty} \gamma_2 = -\infty,
\]

then, for every \(\alpha > 0\), \(\gamma\) intersect the line \(\phi = \alpha\) and so there exists a unique solution to (12)-(14).

\[\square\]

**Lemma 2.** There exists a unique solution \(\phi\) to (16) satisfying the boundary condition \(\phi(0) = a\), for \(a \in (0, \infty]\). Moreover, it is a monotone decreasing function of \(x\).
The proof is similar to that of Lemma 1, therefore we omit the details.

We denote by \( \phi_a \) the solution to (16) satisfying \( \phi(0) = a > 0 \), then

**Lemma 3.** \( \phi_a \in C^\infty(\Omega) \cap H^1(\Omega) \cap L^p(\Omega) \) for \( 1 \leq p \leq \infty \) and

\[
\lim_{a \to \alpha} \| \phi - \phi_a \|_{L^p(\Omega)} = 0, \quad 1 \leq p \leq \infty.
\]

**Proof.** By (18) we deduce that

\[
|\phi_a'(0)|^2 = 2\tilde{\mu}(a + \ln(a + 1 + \tilde{\mu})) + \text{const} < \infty,
\]

which combined with the fact \( \phi > 0 \) (see Lemma 1) we have \( \phi_a' \leq \text{const} \). Multiply (16) by \( \phi_a^p \) and integrate over \((0, \infty)\) to obtain

\[
\phi_a \in L^p(\Omega) \cap H^1(\Omega), \quad \text{for } 1 \leq p < \infty.
\]

\( \phi_a \in L^\infty(\Omega) \) is a consequence of the monotonicity of \( \Phi_a \) and \( 0 < \phi_a \leq a \).

Since \( \phi_a \in W^{1,\infty}(\Omega) \cap H^1(\Omega) \) we have that \( \phi_a \in C(\Omega) \) and then \( \frac{d^2}{dx^2} \phi_a \in C(\Omega) \) and therefore, repeating the process we deduce \( \phi_a \in C^\infty(\Omega) \).

Let \( x_a \) be defined as the unique point in \((0, \infty)\) such that \( \phi_a(x_a) = a \) (i.e. \( x_a := \phi_a^{-1}(a) \)). Notice that

\[
\lim_{a \to \alpha} x_a = 0, \quad (20)
\]

and (by uniqueness of solutions) we have that

\[
\phi_a(x) = \phi(x + x_a). \quad (21)
\]

Then,

\[
\int_0^\infty |\phi - \phi_a| \, dx = \int_0^\infty \phi \, dx - \int_0^\infty \phi_a \, dx = \int_0^\infty \phi \, dx - \int_{x_a}^\infty \phi \, dx = \int_0^{x_a} \phi \, dx \leq x_a \alpha.
\]

Taking limits when \( a \to \alpha \) in the above equation, and by using (20) we obtain

\[
\lim_{a \to \alpha} \int_0^\infty |\phi - \phi_a| \, dx = 0. \quad (22)
\]

(22) proves the lemma for \( p = 1 \). Since \( |\phi - \phi_a|^p \leq |2\alpha|^{p-1} |\phi - \phi_a| \) we have

\[
(\int_0^\infty |\phi - \phi_a|^p \, dx)^{\frac{1}{p}} \leq a^{\frac{p-1}{p}} \left( \int_0^\infty |\phi - \phi_a| \, dx \right)^{\frac{1}{p}},
\]

and taking limits when \( a \to \alpha \) we prove the lemma for \( 1 < p < \infty \).

To prove the case \( p = \infty \) consider the function \( \phi - \phi_a \), by (21) and since \( \phi'' < 0 \) and \( \phi' < 0 \) it results that

\[
\max_{x \in \Omega} \{ \phi - \phi_a \} = \phi(0) - \phi_a(0) = \alpha - a,
\]

and taking limits when \( a \to \alpha \) the proof ends. \( \square \)

4. **Existence, uniqueness and boundary conditions of the solution.** To prove the existence and uniqueness of solutions we first study the boundary conditions of the equation.
4.1. The boundary condition. We consider the system of ODE's

\[
\frac{\partial \pi}{\partial t} = \nu - \pi(1 - \pi) + \pi, \quad t > 0, \tag{23}
\]

\[
\frac{\partial \tau}{\partial t} = \lambda [\pi(1 - \tau) - \mu \pi], \quad t > 0, \tag{24}
\]

with the initial data

\[
\pi = \tau = 0. \tag{25}
\]

**Lemma 4.** There exists a unique solution to (23)-(25) and it satisfies

\[
\lim_{t \to \infty} \pi = \alpha, \quad \lim_{t \to \infty} \tau = \beta;
\]

\[
0 \leq \pi < \frac{\nu + \pi}{1 - \pi}, \quad 0 \leq \tau < \beta, \quad \text{for } t < \infty.
\]

Moreover \( \pi_t \geq 0 \) for \( t > 0 \).

**Proof.** Denote by \( g_1 \) and \( g_2 \) the right hand sides in (23) and (24);

\[
g_1(\pi, \tau) := \nu - \pi(1 - \pi) + \pi, \quad g_2(\pi, \tau) := \lambda [\pi(1 - \tau) - \pi] - \mu \pi.
\]

Since \( g_i \) (for \( i = 1, 2 \)) are \( C^\infty(\mathbb{R}^2) \) there exists \( T_{max} \leq \infty \) such that there exists a unique solution \((\pi, \tau) \in C^\infty(0, T_{max})\) to (23)-(25).

We examine the phase portrait of (23), (24) in the half plane \( \pi \geq 0 \). The unique equilibrium is \((\alpha, \beta)\) and eigenvalues are real and both negative. Then \((\alpha, \beta)\) is locally asymptotically stable.

We consider the region \( B \) defined by

\[
B := \left\{ (\pi, \tau) \in \mathbb{R}^2 \text{ such that } 0 \leq \tau < \beta, \quad 0 \leq \pi < \frac{\nu + \pi}{1 - \pi} \right\}.
\]

Since

- \( \pi' > 0, \tau' < 0 \) at \( \pi = \beta, \quad 0 \leq \pi < \alpha; \)
- \( \pi' = 0, \tau' > 0 \) at \( \pi = \frac{\nu + \pi}{1 - \pi}, \quad 0 \leq \pi < \beta; \)
- \( \pi' > 0, \tau' > 0 \) at \( \pi = 0, \quad 0 \leq \pi < \nu; \)
- \( \pi' > 0, \tau' < 0 \) at \( \pi = 0, \quad 0 \leq \tau < \beta; \)
- \( \pi' > 0, \tau' = 0 \) at \( (0, 0); \)
- \( \pi' > 0, \tau' > 0 \) at \( \pi > 0, \tau < 0; \)
- \( \pi' = 0, \tau' > 0 \) at \( \pi = \nu, \tau = 0; \)

we deduce that the region \( B \) is an invariant region and the solution \((\pi, \tau)\) belongs to \( B \) for \( T_{max} = \infty \) and satisfies

\[
0 \leq \pi < \frac{\nu + \pi}{1 - \pi}, \quad 0 \leq \tau < \beta, \quad \text{for } t < \infty,
\]

\[
\lim_{t \to \infty} \pi = \alpha, \quad \lim_{t \to \infty} \tau = \beta;
\]

and \( \pi_t > 0 \).
4.2. Existence and uniqueness of solutions. We consider the problem (6)-(7) with the boundary conditions

\[ u(0,t) = \pi(t), \quad \lim_{x \to \infty} u(x,t) = 0, \tag{26} \]

where \( \pi(t) \) is the unique solution to (23)-(25).

We first introduce some preliminary Lemmas concerning a priori estimates of the solutions.

**Lemma 5.** \( 0 \leq u \) and \( 0 \leq v \leq 1. \)

**Proof.** Let \( (v-1) \) satisfy

\[ (v-1)_t + (\lambda + \mu + \lambda u)(v-1) = -(\lambda + \mu), \quad t > 0. \]

By integration, we obtain

\[ v(x,t) = 1 - \int_0^t (\lambda + \mu) \exp \left\{ \int_0^\tau (\lambda + \mu + \lambda u(x,s))ds \right\} d\tau - \exp \left\{ - \int_0^t (\lambda + \mu + \lambda u(x,s))d\tau \right\}, \tag{27} \]

which implies

\[ v \leq 1. \tag{28} \]

We introduce the functions \( \psi_\epsilon, \psi, \Psi_\epsilon \) and \( \Psi : \mathbb{R} \to \mathbb{R} \) defined by

\[
\psi_\epsilon(s) := \begin{cases} -1, & s \leq -\epsilon, \\ \frac{1}{2\pi}s, & -\epsilon < s < 0, \\ 0, & s \geq 0, \end{cases} \quad \psi(s) := \begin{cases} -1, & s < 0, \\ 0, & s \geq 0, \end{cases}
\]

\[
\Psi_\epsilon(s) := \begin{cases} -s - \frac{\epsilon}{2}, & s \leq -\epsilon, \\ \frac{1}{2\pi}s^2, & -\epsilon < s < 0, \\ 0, & s \geq 0, \end{cases} \quad \Psi(s) := \begin{cases} -s, & s \leq 0, \\ 0, & s \geq 0, \end{cases}
\]

Notice that \( \Psi' = \psi_\epsilon \) and

\[ \lim_{\epsilon \to 0} \psi_\epsilon = \psi; \quad \lim_{\epsilon \to 0} \Psi_\epsilon = \Psi, \quad s\psi(s) = \Psi(s), \quad \text{for } s \in \mathbb{R}. \]

We multiply (6) by \( \psi_\epsilon(u) \), integrate over \((0,X)\) and take limits as \( X \to \infty \) to get:

\[
\frac{d}{dt} \int_0^\infty \Psi_\epsilon(u)dx + \int_0^\infty \psi_\epsilon'|u|^2dx = \int_0^\infty (-\psi_\epsilon(u)u(1-v) + \psi_\epsilon(u)v)dx,
\]

for \( t > 0 \). Since \( \psi_\epsilon' \geq 0 \), we have

\[
\frac{d}{dt} \int_0^\infty \Psi_\epsilon(u)dx \leq \int_0^\infty (-\psi_\epsilon(u)u(1-v) + \psi_\epsilon(u)v)dx. \tag{31}
\]

Notice that

\[ \lim_{\epsilon \to 0} -\psi_\epsilon(u)u(1-v) - \psi(u)u(1-v) = -\Psi(u)(1-v) \quad \text{a.e.} \]

\[ \lim_{\epsilon \to 0} \psi_\epsilon(u)v = \psi(u)v \leq \Psi(v) \]

and therefore (31) becomes

\[
\frac{d}{dt} \int_0^\infty \Psi(u)dx \leq -\int_0^\infty \Psi(u)(1-v)dx + \int_0^\infty \Psi(v)dx, \quad t > 0. \tag{32}
\]

In the same way we multiply (7) by \( \psi_\epsilon(v) \), integrate over \((0,X)\) and take limits as \( X \to \infty \) to get

\[
\frac{d}{dt} \int_0^\infty \Psi_\epsilon(v)dx = \int_0^\infty (\lambda \psi_\epsilon(v)u(1-v) - \mu \psi_\epsilon(v)v)dx.
\]
We take limits as $\epsilon \to 0$
\[
\frac{d}{dt} \int_0^\infty \Psi(v)dx = \lambda \int_0^\infty \psi(v)u(1-v)dx - \mu \int_0^\infty \Psi(v)dx,
\] (33)
thanks to (28) the inequalities
\[
\psi(v)(1-v) \leq 0,
\]
\[
\psi(v)u(1-v) \leq -\psi(v)\Psi(u)(1-v) \leq \Psi(u)(1-v),
\]
hold and (33) becomes
\[
\frac{d}{dt} \int_0^\infty \Psi(v)dx \leq \lambda \int_0^\infty \Psi(u)(1-v)dx - \mu \int_0^\infty \Psi(v)dx.
\] (34)
We multiply equation (32) by $\lambda$ and add to equation (34) to get
\[
\frac{d}{dt} \left( \lambda \int_0^\infty \Psi(u)dx + \int_0^\infty \Psi(v)dx \right) \leq (\lambda - \mu) \int_0^\infty \Psi(v)dx, \quad \text{for } t > 0.
\]
We apply Gronwall’s lemma to the above equation and the proof ends. □

**Lemma 6.** $u \leq \phi$ and $v \leq \xi$.

**Proof.** Consider $u - \phi, v - \xi$ which satisfy:
\[
(u - \phi)_t - (u - \phi)_{xx} = -(u - \phi)(1-v) + (v - \xi)(1+\phi), \quad x > 0, \quad t > 0,
\] (35)
and
\[
(v - \xi)_t = \lambda(u - \phi)(1-v) - (v - \xi)(\lambda + \mu + \lambda\phi), \quad t > 0.
\] (36)
We introduce the functions $\theta_\epsilon, \theta, \Theta_\epsilon$ and $\Theta$ defined by
\[
\theta_\epsilon(s) := \begin{cases} 
0, & s \leq 0, \\
\frac{1}{\epsilon}s, & 0 < s < \epsilon, \\
1, & s \geq \epsilon,
\end{cases}
\]
(37)
\[
\theta(s) := \begin{cases} 
0, & s < 0, \\
1, & s \geq 0,
\end{cases}
\]
\[
\Theta_\epsilon(s) := \begin{cases} 
0, & s \leq 0, \\
\frac{1}{\epsilon^2}s^2, & 0 < s < \epsilon, \\
\frac{s - 1}{2\epsilon}, & s \geq \epsilon,
\end{cases}
\]
(38)
Notice that $\Theta'_\epsilon = \theta_\epsilon, s\theta(s) = \Theta(s)$ for $s \in \mathbb{R}$ and
\[
\lim_{\epsilon \to 0} \theta_\epsilon = \theta, \quad \lim_{\epsilon \to 0} \Theta_\epsilon = \Theta.
\]
We multiply equation (35) by $\theta_\epsilon(u - \phi)$, integrate over $(0, X)$ and take limits as $X \to \infty$ to get
\[
\frac{d}{dt} \int_0^\infty \Theta_\epsilon(u - \phi)dx + \int_0^\infty \theta_\epsilon'|(u - \phi)_x|^2dx = 
\]
\[
\int_0^\infty (-\theta_\epsilon(u - \phi)(u - \phi)(1-v) + \theta_\epsilon(u - \phi)(v - \xi)(1+\phi)) dx, \quad t > 0.
\]
Since $\theta_\epsilon' \geq 0$, we have, for $t > 0$
\[
\frac{d}{dt} \int_0^\infty \Theta_\epsilon(u - \phi)dx \leq 
\]
\[
\int_0^\infty (-\theta_\epsilon(u - \phi)(u - \phi)(1-v) + \theta_\epsilon(u - \phi)(v - \xi)(1+\phi)) dx.
\]
Taking limits in the above equation, it results
\[
\frac{d}{dt} \int_0^\infty \Theta(u - \phi)dx \leq
\]
\[
- \int_0^\infty \Theta(u - \phi)(1 - v)dx + \int_0^\infty \Theta(u - \phi)(v - \xi)(1 + \phi)dx, \text{ for } t > 0.
\]
(39)

Notice that
\[
\theta(u - \phi)(v - \xi)(1 + \phi) \leq \theta(u - \phi)\Theta(v - \xi)(1 + \phi) \leq \Theta(v - \xi)(1 + \phi)
\]
which, replacing in (39), yields
\[
\frac{d}{dt} \int_0^\infty \Theta(u - \phi)dx \leq - \int_0^\infty \Theta(u - \phi)(1 - v)dx + \int_0^\infty \Theta(v - \xi)(1 + \phi)dx.
\]
(40)

In the same way we multiply (35) by \(\lambda - 1\) and integrate over \((0, X)\) to take limits as \(X \to \infty\)
\[
\lambda^{-1} \frac{d}{dt} \int_0^\infty \Theta(v - \xi)dx =
\]
\[
\int_0^\infty \left( \theta(v - \xi)(u - \phi)(1 - v) - \theta(v - \xi)(v - \xi) \left( 1 + \frac{\mu}{\lambda} + \phi \right) \right) dx.
\]
(41)

Taking limits when \(\epsilon \to 0\) it results
\[
\lambda^{-1} \frac{d}{dt} \int_0^\infty \Theta(v - \xi)dx =
\]
\[
\int_0^\infty \theta(v - \xi)(u - \phi)(1 - v)dx - \int_0^\infty \Theta(v - \xi) \left( 1 + \frac{\mu}{\lambda} + \phi \right) dx
\]
(41)

Since
\[
\theta(v - \xi)(u - \phi)(1 - v) \leq \theta(v - \xi)\Theta(u - \phi)(1 - v) \leq \Theta(u - \phi)(1 - v),
\]
(41) becomes
\[
\lambda^{-1} \frac{d}{dt} \int_0^\infty \Theta(v - \xi)dx \leq
\]
\[
\int_0^\infty \Theta(u - \phi)(1 - v)dx - \int_0^\infty \Theta(v - \xi) \left( 1 + \frac{\mu}{\lambda} + \phi \right) dx,
\]
which, combining with (40), results
\[
\frac{d}{dt} \left( \int_0^\infty \Theta(u - \phi)dx + \lambda^{-1} \int_0^\infty \Theta(v - \xi)dx \right) \leq - \frac{\mu}{\lambda} \int_0^\infty \Theta(v - \xi)dx \leq 0.
\]

Then, by Gronwall’s lemma we obtain
\[
\int_0^\infty \Theta(u - \phi)dx = \int_0^\infty \Theta(v - \xi)dx = 0,
\]
which ends the proof. \(\square\)

**Theorem 1.** There exists a unique solution \((u, v)\) to the problem (6)-(10) satisfying
\[
u \in W^{1,2}(0, \infty; L^2(\Omega)) \cap L^2(0, \infty; H^1(\Omega));
\]
\[
v \in W^{2,2}(0, \infty; L^2(\Omega)) \cap W^{1,2}(0, \infty; H^1(\Omega)).
\]
Proof. Let $T \in (0, \infty)$, $z := e^{-\omega t}(u - \varpi \sigma(x))$, for
\[\omega := \max \left\{ T + \frac{\alpha^2}{2}, \frac{\lambda^2}{2} + \lambda \alpha - \mu - \lambda \right\},\]
and $\sigma(x) \in C^\infty(\Omega)$, such that $\sigma(x) = 1$ in $(0, 1)$ and $\sigma(x) = 0$ for $x > 2$. $z$ satisfies
\[
\frac{\partial z}{\partial t} - \frac{\partial^2 z}{\partial x^2} + (1 + \omega - v)z = (-\varpi \sigma - \varpi \sigma_x - \varpi \sigma(1 - v) + v)e^{-\omega t}, \quad x > 0, \quad t > 0. \tag{42}
\]
where $v$ is the solution of the equation
\[
\frac{\partial v}{\partial t} = \lambda \left[ (e^{\omega t} z + \varpi \sigma)(1 - v) + v \right] - \mu v, \quad t > 0,
\]
with the boundary conditions
\[
z(0, t) = 0, \tag{43}
\]
and initial data
\[
z(x, 0) = v(x, 0) = 0. \tag{44}
\]
By (27) $v$ is given by
\[
v(x, t) = 1 - \int_0^t (1 + \mu) \exp \left\{ \int_t^\tau (\lambda + \mu + \lambda e^{\omega s} z(x, s) + \lambda \varpi(s)\sigma(x)) ds \right\} d\tau - \exp \left\{ - \int_0^t (\lambda + \mu + \lambda e^{\omega s} z(x, s) + \lambda \varpi(s)\sigma(x)) d\tau \right\}. \tag{45}
\]
We denote by $f(t, v)$ the right side part of (42), then the problem (42)-(44) becomes:
\[
\begin{cases}
\frac{\partial z}{\partial t} - \frac{\partial^2 z}{\partial x^2} + (1 + \omega - v)z = f(t, v), & t > 0, \quad x > 0, \\
z(x, 0) = 0, & x > 0, \\
z(0, t) = 0, & t > 0.
\end{cases} \tag{46}
\]
We use the Banach fixed point theorem in order to obtain the existence of solutions for (46). Let $V(\Omega)$ define by
\[
V(\Omega) := \left\{ z \in H^1(\Omega), \text{ such that } z(0) = 0, \| z \|_{V(\Omega)} := \| z_x \|_{L^2(\Omega)} + \| \varpi \|_{L^2(\Omega)} \right\},
\]
for $\varpi := \omega - \frac{\alpha^2}{2} > 0$. Notice that $V(\Omega)$ is a separable Hilbert space and the embeddings
\[V(\Omega) \hookrightarrow L^2(\Omega) \hookrightarrow V'(\Omega),\]
are continuous. Let $A$ be the subset of functions defined by
\[A := \{ z \in L^2(0, T : V(\Omega)); 0 \leq e^{\omega t} z + \varpi \sigma(x) \leq \phi \}.
\]
Let $J : A \to L^2(0, T : V(\Omega))$ be defined by $J(\hat{z}) := z$, where $z$ is the solution to (46) and $v$ is given by
\[
1 - \int_0^t (1 + \mu) \exp \left\{ \int_t^\tau (\lambda + \mu + \lambda e^{\omega s} \hat{z}(x, s) + \lambda \varpi(s)\sigma(x)) ds \right\} d\tau - \exp \left\{ - \int_0^t (\lambda + \mu + \lambda e^{\omega s} \hat{z}(x, s) + \lambda \varpi(s)\sigma(x)) d\tau \right\}. \tag{47}
\]
Since $\hat{z} \in A$, definition of $\sigma$, we have that
\[f \in L^p(\Omega_T) \text{ for } 1 \leq p \leq \infty. \tag{48}
\]
We consider the following:
i. \( v \geq 0 \) and \( v \geq 1 \).

The proof is similar to the proof of Lemma 5 therefore the details are omitted.

ii. \( J \) is well defined.

Since \( f \in L^2(\Omega_T) \) and \( 0 \leq v \leq 1 \) we have that there exists a unique solution \( z \in L^2(0, T : V(\Omega)) \) to (46). See, for instance, Showalter [15] (Proposition 2.3 p.112).

iii. \( 0 \leq ze^{\omega t} + \overline{\pi} \sigma \leq \phi \).

We consider the function \((ze^{\omega t} + \overline{\pi} \sigma - \phi)\) which satisfies the equation
\[
(ze^{\omega t} + \overline{\pi} \sigma - \phi)_t - (ze^{\omega t} + \overline{\pi} \sigma - \phi)_{xx} + (ze^{\omega t} + \overline{\pi} \sigma - \phi)(1 - v) = (v - \xi)(1 + \phi),
\]
and
\[
(v - \xi)_t = \lambda (ze^{\omega t} + \overline{\pi} \sigma - \phi)(1 - v) - (v - \xi)(\lambda + \mu + \lambda \phi).
\]

Consider the functions defined in (37)-(38) and proceed as in Lemmas 5 and 6 to obtain
\[
0 \leq ze^{\omega t} + \overline{\pi} \sigma \leq \phi.
\]

iv. \( J(A) \subset A \).

It is a consequence of (ii) and (iii).

v. \( J \) is a contraction.

Let \( \hat{z}_1, \in A, \ z_i := J(\hat{z}_i) \) and \( v_i \) defined by
\[
v_i := 1 - \int_0^1 (\lambda + \mu) \exp \left\{ \int_t^1 (\lambda + \mu + \lambda e^{\omega t} \hat{z}_i(x, s) + \lambda \overline{\pi}(s) \sigma(x) ) ds \right\} d\tau - \\
\exp \left\{ - \int_0^1 (\lambda + \mu + \lambda e^{\omega t} \hat{z}_i(x, s) + \lambda \overline{\pi}(s) \sigma(x) ) d\tau \right\}, \quad \text{for } i = 1, 2.
\]

Let us define \( Z := z_1 - z_2, V := v_1 - v_2 \) and \( \hat{Z} := \hat{z}_1 - \hat{z}_2 \), then
\[
\frac{\partial}{\partial \sigma} Z - \frac{\partial^2}{\partial x^2} Z + (1 + \omega) Z = V(e^{-\omega t} + z_1 + e^{-\omega t} \overline{\pi} \sigma) + Z v_2, \quad \text{in } \Omega_T,
\]
\[
\frac{\partial}{\partial \pi} V = \lambda \left[ \hat{Z} e^{\omega t} (1 - v_1) - V(1 - \hat{z}_2 e^{\omega t} - \overline{\pi} \sigma) \right] - \mu V, \quad \text{in } \Omega_T.
\]

Multiply the system by \((Z, V)\) and after integration over \( \Omega \)
\[
\frac{d}{dt} \frac{1}{2} \int_0^\infty Z^2 dx + \int_0^\infty \left| \frac{\partial}{\partial x} Z \right|^2 dx + \int_0^\infty (1 + \omega - v_2) |Z|^2 dx = \\
e^{-\omega t} \int_0^\infty Z V(1 + e^{\omega t} z_1 + \overline{\pi} \sigma) dx,
\]
and
\[
\frac{d}{dt} \frac{1}{2} \int_0^\infty V^2 dx = \int_0^\infty \left[ \lambda V \hat{Z} e^{\omega t} (1 - v_1) - V^2 (\mu + \lambda (1 - \hat{z}_2 e^{\omega t} - \overline{\pi} \sigma)) \right] dx.
\]

Then
\[
\frac{d}{dt} \frac{1}{2} \int_0^\infty Z^2 dx + \int_0^\infty \left[ \left| \frac{\partial}{\partial x} Z \right|^2 + (1 + \omega) |Z|^2 \right] dx \leq e^{-\omega t} \int_0^\infty ZV \phi dx, \quad (50)
\]
and
\[
\frac{d}{dt} \frac{1}{2} \int_0^\infty V^2 dx + (\mu + \lambda) \int_0^\infty V^2 dx \leq \int_0^\infty \left[ \lambda e^{\omega t} V \hat{Z} + \lambda V^2 \phi \right] dx. \quad (51)
\]

Notice that,
\[
e^{-\omega t} \int_0^\infty ZV \phi dx \leq e^{-\omega t} \alpha \int_0^\infty ZV dx \leq \int_0^\infty \left[ \frac{\alpha^2}{2} Z^2 + \frac{e^{-2\omega t}}{2} V^2 \right] dx, \quad (52)
\]
and
\[ \int_0^\infty \left[ \lambda e^{\omega t} \dot{Z} + \lambda V^2 \phi \right] dx \leq \left( \frac{\lambda^2}{2} + \lambda \alpha \right) \int_0^\infty V^2 dx + \frac{e^{2\omega t}}{2} \int_0^\infty \dot{Z}^2 dx. \]  \hspace{1cm} (53)

Since \( \omega \geq \frac{\lambda^2}{2} + \lambda \alpha - \mu - \lambda \), (51) and (53) imply
\[ \frac{d}{dt} \left( \int_0^\infty V^2 dx \right) \leq \omega \int_0^\infty V^2 dx + \frac{e^{2\omega t}}{2} \int_0^\infty \dot{Z}^2 dx, \]

by Gronwall’s lemma we have
\[ \int_0^\infty V^2 dx \leq e^{2\omega t} \int_0^t \int_0^\infty \dot{Z}^2 dx ds. \] \hspace{1cm} (54)

By (50), (52) and (54) we deduce
\[ \frac{d}{dt} \int_0^\infty Z^2 dx + \int_0^\infty \left[ \left| \frac{\partial}{\partial x} Z \right|^2 + \left( 1 + \omega - \frac{\alpha^2}{2} \right) |Z|^2 \right] dx \leq \int_0^t \int_0^\infty \dot{Z}^2 dx ds. \]

We integrate over \((0, T)\) to get
\[ \int_{\Omega_T} \left| \frac{\partial}{\partial x} Z \right|^2 dx + \left( 1 + \omega - \frac{\alpha^2}{2} \right) \int_{\Omega_T} |Z|^2 dx \leq \frac{T}{2} \int_{\Omega_T} \dot{Z}^2 dx ds. \]

Since \( \omega = \omega - \frac{\alpha^2}{2} \geq T \) we have that
\[ \|Z\|_{L^2(0,T;V(\Omega))} \leq \frac{1}{2} \|\dot{Z}\|_{L^2(0,T;V(\Omega))}, \]

which implies that \( T \) is a contraction.

vi. Thanks to i-v we apply Banach fixed point theorem to obtain the existence and uniqueness of solution
\[ z \in L^2(0,T;V(\Omega)) \cap W^{1,2}(0,T;L^2(\Omega)) \]
to (46) for \( T < \infty \). Doing the change of unknown \( u = e^{\omega t}z + \bar{\omega}\sigma \) the proof ends.

\[ \square \]

5. Asymptotic behavior of the solution.

**Theorem 2.** The solution \((u, v)\) to (6)-(10) satisfies
\[ \lim_{t \to \infty} u(x,t) = \phi(x), \quad \lim_{t \to \infty} v(x,t) = \xi(x), \quad \text{in } L^p(\Omega) \quad \text{for } 1 \leq p < \infty, \]
where \((\phi, \xi)\) is the steady state of (12)-(14).

**Proof.** We first consider the following:

- \( a \in (0, \alpha] \);
- \( x_a \) is defined as the unique point in the interval \((0, \infty)\) such that \( \phi(x_a) = a \), (i.e. \( x_a := \phi^{-1}(a) \)). Notice that \( x_0 = 0 \) and \( \lim_{a \to 0} x_a = \infty \) (see Lemma 2);
- \( b := \xi(x_a) \), \( b \in (0, \beta] \);
- \( \phi_a(x) := \phi(x + x_a) \). Notice that \( \phi_a \) is a solution to (14) satisfying \( \phi_a(0) = a \) (see Lemma 2);
- \( \xi_a := \frac{\phi_a}{1 + \mu + \phi_a} \);
\begin{itemize}
\item \( T_a \) is defined as the unique point in the interval \((0, \infty)\) such that \( \Omega(T_a) = a \) (i.e. \( T_a := \Omega^{-1}(a) \));
\item \( T_b \) is defined as the unique point in the interval \((0, \infty)\) such that \( \Omega(T_b) = b \) (i.e. \( T_b := \Omega^{-1}(b) \));
\item \( T_{ab} := \max\{T_a, T_b\} \).
\end{itemize}

Notice that \((\phi_a, \xi_a)\) is a solution to \((12), (13)\) and it satisfies \( \phi_a(0) = a, \xi_a(0) = b. \)
Then \( u - \phi_a \) and \( v - \xi_a \) satisfy
\[
(u - \phi_a)_t - (u - \phi_a)_xx = -(u - \phi_a)(1 - v) + (v - \xi_a)(1 + \phi_a), \quad x > 0, \quad t > T_{ab}; \quad (55)
\]
and
\[
(v - \xi_a)_t = \lambda(u - \phi_a)(1 - v) - (v - \xi_a)(\lambda + \mu + \lambda \phi_a), \quad x > 0, \quad t > T_{ab}. \quad (56)
\]

We consider the functions \( \psi_{\epsilon}, \psi, \Psi_{\epsilon} \) and \( \Psi \) defined in \((29), (30)\) and multiply \((55)\) by \( \psi_{\epsilon}(u - \phi_a) \). After integration over \((0, X)\) we take limits when \( X \to \infty \) to get
\[
\frac{d}{dt} \int_0^\infty \Psi_{\epsilon}(u - \phi_a) \, dx + \int_0^\infty \psi_{\epsilon}'(u - \phi_a)_x^2 \, dx =
\int_0^\infty (-\psi_{\epsilon}(u - \phi_a)(u - \phi_a)(1 - v) + \psi_{\epsilon}(u - \phi_a)(v - \xi_a)(1 + \phi_a)) \, dx,
\]
for \( t > T_{ab} \). Since \( \psi_{\epsilon}' \geq 0 \), we have
\[
\frac{d}{dt} \int_0^\infty \Psi_{\epsilon}(u - \phi_a) \, dx \leq
\int_0^\infty (-\psi_{\epsilon}(u - \phi_a)(u - \phi_a)(1 - v) + \psi_{\epsilon}(u - \phi_a)(v - \xi_a)(1 + \phi_a)) \, dx.
\]

Taking limits as \( \epsilon \to 0 \) and using \( 0 \leq v < \xi \leq \beta < 1 \) and \( \phi_a > 0 \), we obtain
\[
\frac{d}{dt} \int_0^\infty \Psi(u - \phi_a) \, dx \leq \int_0^\infty -\Psi(u - \phi_a)(1 - v) \, dx +
\int_0^\infty \psi(u - \phi_a)(v - \xi_a)(1 + \phi_a) \, dx, \quad \text{for} \ t > T_{ab}.
\]

Notice that
\[
\psi(u - \phi_a)(v - \xi)(1 + \phi_a) \leq -\psi(u - \phi_a)\Psi(v - \xi_a)(1 + \phi_a) \leq \Psi(v - \xi_a)(1 + \phi_a),
\]
which implies
\[
\frac{d}{dt} \int_0^\infty \Psi(u - \phi_a) \, dx \leq \int_0^\infty -\Psi(u - \phi_a)(1 - v) \, dx + \int_0^\infty \Psi(v - \xi)(1 + \phi_a) \, dx, \quad (57)
\]
for \( t > T_{ab} \). In the same way we multiply \((56)\) by \((1 - \delta)\psi_{\epsilon}(v - \xi_a)\), for \( \delta \) given by
\[
\delta := \frac{\mu}{2(\lambda + \mu + \lambda \alpha)},
\]
and \( \alpha \) defined by \((15)\). We integrate over \( \Omega \) to obtain
\[
(1 - \delta) \frac{d}{dt} \int_0^\infty \Psi_{\epsilon}(v - \xi_a) \, dx = (1 - \delta) \int_0^\infty \lambda \psi_{\epsilon}(v - \xi_a)(u - \phi_a)(1 - v) \, dx
\]
\[
- (1 - \delta) \int_0^\infty \psi_{\epsilon}(v - \xi_a)(v - \xi_a)(\lambda + \mu + \lambda \phi_a) \, dx, \quad \text{for} \ t > T_{ab},
\]
and taking limits when $\epsilon \to 0$ it results:

$$(1 - \delta) \frac{d}{dt} \int_0^\infty \Psi(v - \xi_a)dx = (1 - \delta) \int_0^\infty \lambda \psi(v - \xi_a)(u - \phi_a)(1 - v)dx$$

$$-(1 - \delta) \int_0^\infty \Psi(v - \xi_a)(\lambda + \mu + \lambda \phi_a)dx,$$ for $t > T_{ab}$.

Since

$$\psi(v - \xi_a)(u - \phi_a)(1 - v) \leq -\psi(v - \xi_a)\Psi(u - \phi_a)(1 - v) \leq \Psi(u - \phi_a)(1 - v),$$

it results

$$(1 - \delta) \frac{d}{dt} \int_0^\infty \Psi(v - \xi_a)dx \leq (1 - \delta) \int_0^\infty \lambda \psi(v - \xi_a)(1 - v)dx$$

$$- (1 - \delta) \int_0^\infty \Psi(v - \xi_a)(\lambda + \mu + \lambda \phi_a)dx,$$ for $t > T_{ab}$. (58)

Combining (57) with (58) we get

$$\frac{d}{dt} \left( \int_0^\infty \Psi(u - \phi_a)dx + (1 - \delta) \int_0^\infty \Psi(v - \psi_a)dx \right) \leq$$

$$- \delta \int_0^\infty \lambda \Psi(u - \phi_a)(1 - v)dx - \int_0^\infty \Psi(v - \xi_a)((1 - \delta)\mu - \delta \lambda(1 + \phi_a))dx,$$ for $t > T_{ab}$. Since $\delta = \frac{\mu}{2(\lambda + \mu + \lambda \alpha)}$ and $\phi_a \leq \alpha$,

$$(1 - \delta)\mu - \lambda \delta(1 + \phi_a) \geq (1 - \delta)\mu - \lambda \delta(1 + \alpha) = \mu - \delta(\lambda + \mu + \lambda \alpha) = \frac{\mu}{2}.$$

Then, from (59), since $(1 - v) \leq 1 - \beta$ we have

$$\frac{d}{dt} \left( \int_0^\infty \Psi(u - \phi_a)dx + (1 - \delta) \int_0^\infty \Psi(v - \xi_a)dx \right) \leq$$

$$- \delta(1 - \beta) \int_0^\infty \Psi(u - \phi_a)dx - \frac{\mu}{2} \int_0^\infty \Psi(v - \xi_a)dx,$$ for $t > T_{ab}$.

Let $c_6 := \min \left\{ \delta(1 - \beta), \frac{\mu}{2(1 - \delta)} \right\}$, then, by Gronwall’s lemma we obtain

$$\left( \int_0^\infty \Psi(u - \phi_a)dx + (1 - \delta) \int_0^\infty \Psi(v - \xi_a)dx \right) \leq$$

$$\left( \int_0^\infty \phi_a dx + (1 - \delta) \int_0^\infty \xi_a dx \right) e^{-c_6 t}.$$

Since

$$|\phi(x) - u(x, t)| \leq |\phi(x) - \phi_a(x)| + \Psi(u(x, t) - \phi_a(x)),$$

and

$$|\xi(x) - v(x, t)| \leq |\xi(x) - \xi_a(x)| + \Psi(v(x, t) - \xi_a(x)),$$

we have, in view of Lemma (3), that

$$\int_0^\infty |\phi - u|dx + \int_0^\infty |\xi - v|dx \leq$$

$$\int_0^\infty (|\phi - \phi_a| + |\xi - \xi_a|) dx + \int_0^\infty (\Psi(u - \phi_a) + \Psi(v - \xi_a)) dx \leq$$
\[
\int_0^\infty (|\phi - \phi_a| + |\xi - \xi_a|)dx + c_T e^{-ct_a} t \leq \left( \alpha + \frac{\alpha}{1 + \mu + \alpha} \right) x_a + c_T e^{-ct_a}. \tag{60}
\]

Then
\[
\lim_{t \to -\infty} \int_0^\infty |\phi - u| dx + \int_0^\infty |\xi - v| dx = \lim_{T_{ab} \to -\infty} \int_0^\infty |\phi - u| dx + \int_0^\infty |\xi - v| dx \leq \left( \alpha + \frac{\alpha}{1 + \mu + \alpha} \right) x_a + c_T e^{-ct_a T_{ab}} = 0,
\]
which completes the proof for \( p = 1 \). The case \( 1 < p < \infty \) is a consequence of the inequalities
\[
\|u - \phi\|_{L^p(\Omega)} \leq \|u - \phi\|_{L^\infty(\Omega)} \|u - \phi\|_{L^p(\Omega)} \leq \alpha \frac{e^\mu}{p} \|u - \phi\|_{L^1(\Omega)}, \tag{61}
\]
\[
\|v - \xi\|_{L^p(\Omega)} \leq \|v - \xi\|_{L^\infty(\Omega)} \|v - \xi\|_{L^p(\Omega)} \leq \beta \frac{e^\mu}{p} \|v - \xi\|_{L^1(\Omega)} \tag{62}
\]
and (60).

6. The problem with receptors and bound receptors. In the mathematical model proposed by Lander, Nie and Wan [6] assumption (1) reduces the number of equations and simplifies the system. Degradation of the products has to be considered to study the problem for large intervals of time. Lander, Nie, Vargas and Wan [8] do not consider assumption (1) and propose a system of three equations: a PDE morphogens concentration \([L]\), and two ODE’s for bound receptors and free receptors, \([LR]\) and \([R]\) respectively. The problem is studied in a bounded domain \( I = (X_{min}, X_{max}) \) and the system is the following (see [8])
\[
\frac{\partial}{\partial t}[L] - \frac{d}{dx} \frac{\partial}{\partial x}[L] = -k_{on}[L][R] + k_{off}[LR] + v_L(x, t), \quad x \in I, \ t > 0,
\]
\[
\frac{\partial}{\partial t}[LR] = k_{on}[L][R] - (k_{off} + k_{deg})[LR], \quad x \in I, \ t > 0,
\]
\[
\frac{\partial}{\partial t}[R] = v_R(x, t) - k_{on}[L][R] + k_{off}[LR] - k_{deg}[R], \quad x \in I, \ t > 0,
\]
for
\[
v_L(x, t) := \begin{cases} k_v, & \text{for } x \geq 0, \\ 0, & \text{for } x \leq 0; \end{cases} \quad v_R(x, t) := k_R.
\]
The system is completed with the boundary conditions
\[
\frac{\partial}{\partial x}[L] = 0, \text{ at } x = X_{min}, \ t > 0; \quad [L] = 0, \text{ at } x = X_{max}, \ t > 0.
\]
We assume that the initial distribution of receptors is constant, i.e.
\[
[R(0, x)] = R_{tot},
\]
and
\[
[L] = [LR] = 0, \quad \text{at } t = 0, \quad x \in I.
\]
Instead of considering a bounded domain we propose, as in previous sections, to work in \( \Omega := \{ x \in R; \ x > 0 \} \) and that morphogens are synthesized at \( x = 0 \). Then, the above system becomes:
\[
\frac{\partial}{\partial t}[L] - \frac{d}{dx} \frac{\partial}{\partial x}[L] = -k_{on}[L][R] + k_{off}[LR], \quad x > 0, \ t > 0,
\]
\[
\frac{\partial}{\partial t}[LR] = k_{on}[L][R] - (k_{off} + k_{deg})[LR], \quad x > 0, \ t > 0,
\]
\[
\frac{\partial}{\partial t}[R] = k_R - k_{on}[L][R] + k_{off}[LR] - k_{deg}[R], \quad x > 0, \ t > 0,
\]
with the boundary conditions:
\[ \partial_t[L] = k_{syn} - k_{on}[L][R] + k_{off}[LR], \text{ at } x = 0, \quad t > 0, \quad \lim_{x \to \infty} [L] = 0, \]
and the initial data:
\[ [L] = [LR] = 0, \quad [R] = R_0 \quad \text{at } t = 0, \quad x \in \Omega. \]

We introduce the dimensionless variables:
\[ \tilde{t} := k_{on} R_{tot} t; \quad \tilde{x} := \left( \frac{k_{on} R_{tot}}{d} \right)^{1/2} x; \]
\[ u := \frac{k_{on}}{k_{off}} [L]; \quad v := \frac{[LR]}{R_{tot}}; \quad w := \frac{[R]}{R_{tot}}; \]
the parameters defined in Section 2
\[ \mu := \frac{k_{deg}}{k_{off} R_{tot}}; \quad \lambda := \frac{k_{off}}{k_{on} R_{tot}}; \quad \nu := \frac{k_{syn}}{k_{off} R_{tot}}, \]
and the new parameters
\[ \kappa := \frac{k_R}{R_{tot} k_{on}}; \quad \eta := \frac{k_{deg}}{R_{tot} k_{on}}. \]

In terms of the new variables and parameters the dimensionless version of the model is the following:
\[ \begin{align*}
\frac{\partial}{\partial t} u - \frac{\partial^2}{\partial x^2} u &= -uw + v, \quad x > 0, \quad t > 0, \\
\frac{\partial}{\partial t} v &= \lambda(uw - v) - \mu v, \quad x > 0, \quad t > 0, \\
\frac{\partial}{\partial t} w &= \kappa - \lambda(uw - v) - \eta w, \quad x > 0, \quad t > 0,
\end{align*} \tag{63} \]
with the boundary conditions:
\[ \begin{align*}
\frac{\partial}{\partial t} u &= \nu - uw + v, \quad \text{at } x = 0, \quad t > 0, \quad \lim_{x \to \infty} u = 0, \\
\text{and the initial data:} \quad u &= v = 0, \quad w = 1 \quad \text{at } t = 0, \quad x \in \Omega. \tag{67}
\end{align*} \]
For technical reasons we assume through this section that
\[ \mu \kappa - \nu > 0. \tag{68} \]

6.1. **The steady states.** The steady states of the problem are given by the system:
\[ \begin{align*}
- \frac{\partial^2}{\partial x^2} u &= -uw + v, \quad x > 0, \\
0 &= \lambda(uw - v) - \mu v, \quad x > 0, \\
0 &= \kappa - \lambda(uw - v) - \eta w, \quad x > 0,
\end{align*} \tag{69} \]
with the boundary conditions:
\[ \begin{align*}
0 &= \nu - uw + v, \quad \text{at } x = 0, \quad t > 0; \quad \lim_{x \to \infty} u = 0. \tag{72}
\end{align*} \]
Combine (70) with (71) to obtain
\[ w = \frac{\kappa}{\eta} - \frac{\mu}{\eta} v, \]
which, combined with (70), yields

\[ 0 = \lambda u \left( \frac{\kappa}{\eta} - \frac{\mu}{\eta} \right) - (\lambda + \mu)v. \]

Then

\[ v \left( \frac{\lambda\mu}{\eta} u + \lambda + \mu \right) = \frac{\kappa\lambda}{\eta} u, \]

and hence

\[ \mu v = \frac{\lambda\kappa u}{\lambda u + \frac{\lambda u + \mu}{\mu}} = \frac{\kappa u}{u + \frac{\mu}{\mu} + \frac{\mu}{\mu}}. \]

We denote by \( k_1 \) the following constant

\[ k_1 := \frac{\eta}{\mu} + \frac{\eta}{\lambda}, \tag{73} \]

and equations (69)-(71) become

\[ -\frac{\partial^2}{\partial x^2} u + \kappa \frac{u}{u + k_1} = 0. \tag{74} \]

Combining (72) with (71) we get

\[ 0 = \nu - \kappa \frac{u(0)}{u(0) + k_1}, \]

hence, the boundary conditions for (74) are the following

\[ u(0) = \frac{\nu k_1}{\kappa - \nu} := \tilde{\alpha}, \quad \lim_{x \to \infty} u(x) = 0. \tag{75} \]

By assumption (68) we have that

\[ \tilde{\alpha} > 0. \]

The solution to (74)-(75) have been studied in Section 3 of the present work.

REFERENCES


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