

A model of morphogen transport in the presence of glypicans III

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Abstract

We analyse a stationary problem for the two dimensional model of morphogen transport introduced by Hufnagel et al. The model consists of one linear elliptic PDE posed on $(-1, 1) \times (0, h)$ which is coupled via a nonlinear boundary condition with a nonlinear elliptic PDE posed on $(-1, 1) \times \{0\}$. The main result is that the system has a unique steady state for all ranges of parameters present in the system. Moreover we consider the problem of the dimension reduction. After introducing an appropriate scaling in the model we prove that, as $h \rightarrow 0$, the stationary solution converges to the unique steady state of the one dimensional simplification of the model which was analysed in the first part of the paper. The main difficulty in obtaining appropriate estimates stems from the presence of a measure source term in the boundary condition.

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1 Introduction

Morphogens are signalling molecules which govern the process of cell differentiation in living organisms. They spread from a source spatially localised in the tissue and after a certain amount of time form stable gradients of concentrations. Then receptors located on the surfaces of the cells detect levels of those concentrations and through intracellular pathways this information is conveyed to the nuclei, where the process of gene expression is initiated (see [15]).

The exact mechanism of morphogen transport is still discussed in the literature (see [7], [8], [9] for modelling and [5], [6], [10], [13], [14] for mathematical analysis). A model proposed in [4] accounts for the transport of morphogen Wingless (Wg) in the imaginal wing disc of the *Drosophila Melanogaster*. The present paper is the third part of a series of papers where we analyse mathematical properties of this model, which we call **[HKCS]**. Model **[HKCS]** has two counterparts - two and one dimensional (denoted respectively **[HKCS].2D** and **[HKCS].1D**), depending on the dimension of the domain representing the imaginal wing disc. The main goal of our analysis is a rigorous justification of the so called dimension reduction - **[HKCS].1D** can be obtained from **[HKCS].2D** due to shrinking of the rectangular domain in the direction which corresponds to the thickness of the wing disc.

Model **[HKCS].2D** accounts for the movement of morphogen molecules by (linear) diffusion in the whole domain $\Omega_h = (-1, 1) \times (0, h)$, where $h \ll 1$ denotes thickness of the disc, while being secreted from a point source localised at $x = 0$ on part of the boundary of the wing disc - $\partial_1 \Omega_h = (-1, 1) \times \{0\}$. Moreover association-dissociation reactions of morphogen with receptors and glypicans localised on $\partial_1 \Omega_h$ are

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taken under consideration. After association of morphogen with a receptor (resp. glypican) a morphogen-receptor (resp. -glypican) complex is being formed. Apart of the association-dissociation mechanism glypicans also pass among themselves morphogen molecules, which is realised by introducing diffusion of morphogen-glypican complexes along $\partial_1\Omega_h$. Finally morphogen-glypican complexes can further associate with free receptors creating a triple morphogen-glypican-receptor complexes (which are immotile, similarly as morphogen-receptor complexes). Model **[HKCS].1D** accounts for the same set of reactions between morphogen, glypican and complexes as **[HKCS].2D**. However it is assumed that the imaginal wing disc is completely flat ($h = 0$) so that the whole dynamics takes place only on $\partial_1\Omega_h$.

In [11] - the first part of our study, we proved that **[HKCS].1D** is globally well-posed and has a unique steady state. Article [12] is devoted to the analysis of the evolutionary problem **[HKCS].2D**. Apart of proving global well-posedness we showed that time dependent solutions of **[HKCS].2D**, when properly normalised, converge as $h \rightarrow 0$ to solutions of **[HKCS].1D**. In this paper we turn our attention to the stationary problem associated with **[HKCS].2D**. We prove that there is a unique steady state which converges to the equilibrium of **[HKCS].1D** as $h \rightarrow 0$. We illustrate our result by performing numerical computations which show that the graph of the stationary solution to **[HKCS].2D** becomes homogeneous in x_2 direction as $h \rightarrow 0$. It is worth underlying that all our results are proved without imposing any artificial conditions on the parameters which are present in the system.

1.1 The **[HKCS].2D** model.

In this section we recall model **[HKCS].2D** in a nondimensional form. The model was described in full detail and analysed for the evolutionary case in [12]. For the presentation and analysis of **[HKCS].1D** - a one dimensional simplification we refer to [11]. **[HKCS].2D** in a nondimensional form reads:

$$\partial_t u_1^h + \operatorname{div}(J_h(u_1^h)) = -b_1 u_1^h, \quad (t, x) \in \Omega_T \quad (1a)$$

$$\partial_t u_2^h - d\partial_{x_1}^2 u_2^h = c_1 u_1^h - (b_2 + c_2 + c_3 u_3^h) u_2^h + c_5 u_5^h, \quad (t, x) \in (\partial_1\Omega)_T \quad (1b)$$

$$\partial_t u_3^h = -(b_3 + u_1^h + c_3 u_2^h) u_3^h + c_4 u_4^h + c_5 u_5^h + p_3, \quad (t, x) \in (\partial_1\Omega)_T \quad (1c)$$

$$\partial_t u_4^h = u_1^h u_3^h - (b_4 + c_4) u_4^h, \quad (t, x) \in (\partial_1\Omega)_T \quad (1d)$$

$$\partial_t u_5^h = c_3 u_2^h u_3^h - (b_5 + c_5) u_5^h, \quad (t, x) \in (\partial_1\Omega)_T \quad (1e)$$

with boundary and initial conditions

$$-J_h(u_1^h)\nu = 0, \quad (t, x) \in (\partial_0\Omega)_T$$

$$-J_h(u_1^h)\nu = -(c_1 + u_3^h)u_1^h + c_2 u_2^h + c_4 u_4^h + p_1 \delta, \quad (t, x) \in (\partial_1\Omega)_T$$

$$\partial_{x_1} u_2^h = 0, \quad (t, x) \in (\partial\partial_1\Omega)_T$$

$$\mathbf{u}^h(0, \cdot) = \mathbf{u}_0,$$

where

- $\Omega = (-1, 1) \times (0, 1)$, $\partial\Omega = \partial_0\Omega \cup \partial_1\Omega$, $\partial_1\Omega = (-1, 1) \times \{0\}$, $0 < T \leq \infty$, $\Omega_T = (0, T) \times \Omega$,
- $h > 0$ corresponds to the thickness of the wing disc, $J_h(u) = -(\partial_{x_1} u, h^{-2}\partial_{x_2} u)$,
- ν denotes the outer normal unit vector to $\partial\Omega$,
- δ denotes a one dimensional Dirac Delta i.e $\delta(\phi) = \phi(0)$ for any $\phi \in C([-1, 1])$.

In (1) u_1, u_2, u_3, u_4 and u_5 denote concentrations of free morphogen, morphogen-glypican complexes, free receptors, morphogen-receptor complexes and morphogen-glypican-receptor complexes; c_i 's are rates of reactions between u_i 's; b_1, b_2 denote rates of degradations of u_1, u_2 while b_3, b_4, b_5 are rates of internalisation

of u_3, u_4 and u_5 . Finally d is the diffusion rate of u_2 along $\partial_1\Omega$ while p_1, p_3 denote rates of production of morphogen and free receptors. Notice the dependence of $J_h(u)$ on parameter h .

From now on we impose the following natural assumptions on the signs of constant parameters

$$d, \mathbf{b} > 0, \mathbf{c}, \mathbf{p} \geq 0, \tag{2}$$

where $\mathbf{b} = (b_1, \dots, b_5)$ and similarly for \mathbf{c}, \mathbf{p} .

1.2 Notation

In the whole article $\Omega = (-1, 1) \times (0, 1)$ and $I = (-1, 1)$ are fixed domains. If U is an open subset of \mathbb{R}^n and $1 \leq p \leq \infty$, $s \in \mathbb{R}$, we denote by $W_p^s(U)$ the fractional Sobolev (also known as Sobolev-Slobodecki) spaces and by $\mathcal{M}(U)$ the Banach space of finite, signed Radon measures on \bar{U} equipped with the total variation norm - $\|\cdot\|_{TV}$.

In various estimates we will use a generic constant C which may take different values even in the same paragraph. Constant C may depend on various parameters, but it will never depend on h .

If X is a normed space we denote by X^* its topological dual. Furthermore if $x \in X$ and $x^* \in X^*$ we denote by $\langle x^*, x \rangle_{(X^*, X)} = x^*(x)$ a natural pairing between X and its dual. If H is a Hilbert space we denote by $(\cdot | \cdot)_H$ its scalar product. In particular $(\mathbf{x} | \mathbf{y})_{\mathbb{R}^n} = \sum_{i=1}^n x_i y_i$ and $(f | g)_{L_2(U)} = \int_U fg$. To get more familiar with the notation observe that, due to Riesz theorem, for any $x^* \in H^*$ there exists a unique $x \in H$ such that $\langle x^*, y \rangle_{(H^*, H)} = (x | y)_H$ for all $y \in H$.

2 Results

Let us observe that due to the presence of three ODE's in the system (1), the stationary problem may be reduced to a system of two elliptic equations:

$$\operatorname{div}(J_h(u_1)) + b_1 u_1 = 0, \quad x \in \Omega \tag{3a}$$

$$-d \partial_{x_1}^2 u_2 - c_1 u_1 + (b_2 + c_2 + k_2 H(u_1, u_2)) u_2 = 0, \quad x \in \partial_1 \Omega \tag{3b}$$

with boundary conditions

$$-J_h(u_1)\nu = 0, \quad x \in \partial_0 \Omega \tag{4a}$$

$$-J_h(u_1)\nu = -(c_1 + k_1 H(u_1, u_2)) u_1 + c_2 u_2 + p_1 \delta, \quad x \in \partial_1 \Omega \tag{4b}$$

$$\partial_{x_1} u_2 = 0, \quad x \in \partial \partial_1 \Omega, \tag{4c}$$

where

$$k_1 = b_4 / (b_4 + c_4), \quad k_2 = c_3 b_5 / (b_5 + c_5), \quad H(u_1, u_2) = p_3 / (k_1 u_1 + k_2 u_2 + b_3) \tag{5}$$

and

$$u_3 = H(u_1, u_2), \quad u_4 = \frac{k_1}{b_4} u_1 H(u_1, u_2), \quad u_5 = \frac{k_2}{b_5} u_2 H(u_1, u_2).$$

We will prove the following two theorems

Theorem 1. For every $h \in (0, 1]$ system (3)-(4) has a unique nonnegative W_1^1 solution (u_1^h, u_2^h) i.e. there exists a unique nonnegative $(u_1^h, u_2^h) \in W_1^1(\Omega) \times W_1^1(\partial_1\Omega)$ such that for every $(v_1, v_2) \in W_\infty^1(\Omega) \times W_\infty^1(\partial_1\Omega)$

$$-\int_{\Omega} [J_h(u_1)\nabla v_1 + b_1 u_1 v_1] = p_1 v_1(0) + \int_{\partial_1\Omega} [-(c_1 + k_1 H(u_1, u_2))u_1 + c_2 u_2] v_1, \quad (6a)$$

$$\int_{\partial_1\Omega} d\partial_{x_1} u_2 \partial_{x_1} v_2 = \int_{\partial_1\Omega} [c_1 u_1 - (b_2 + c_2 + k_2 H(u_1, u_2))u_2] v_2. \quad (6b)$$

Moreover $(u_1^h, u_2^h) \in W_p^1(\Omega) \times W_q^2(\partial_1\Omega)$ for every $1 \leq p < 2, 1 \leq q < \infty$ and

$$\|u_1^h\|_{W_p^1(\Omega)} + h^{-1} \|\partial_{x_2} u_1^h\|_{L_p(\Omega)} + \|u_2^h\|_{W_q^2(\partial_1\Omega)} \leq C, \quad (7)$$

where C does not depend on h .

Theorem 2. Let (u_1^h, u_2^h) be the unique solution of system (3)-(4). Then for every $1 \leq p < 2, 1 \leq q < \infty$ we have the following weak convergence as $h \rightarrow 0^+$

$$u_1^h \rightharpoonup u_1^0 \quad \text{in } W_p^1(\Omega), \quad (8a)$$

$$u_2^h \rightharpoonup u_2^0 \quad \text{in } W_q^2(\partial_1\Omega). \quad (8b)$$

Moreover $\partial_{x_2} u_1^0 = 0$ (so that u_1^0 depends only on x_1) and $(u_1^0, u_2^0) \in W_\infty^1(I) \times C^2(\bar{I})$ is the unique solution of

$$-u_1'' + (b_1 + c_1 + k_1 H(u_1, u_2))u_1 - c_2 u_2 = p_1 \delta, \quad x \in I \quad (9a)$$

$$-du_2'' - c_1 u_1 + (b_2 + c_2 + k_2 H(u_1, u_2))u_2 = 0, \quad x \in I \quad (9b)$$

$$u_1' = u_2' = 0, \quad x \in \partial I. \quad (9c)$$

Remark 1. Notice that (9) is the stationary problem associated with model [HKCS].1D (analysed previously in [11]). Thus Theorem (2) is the rigorous formulation of the dimension reduction of the model [HKCS].2D in the stationary case.

On Figure (1) we present graphs of u_1^h for several values of h . Notice that as h becomes smaller the graph of u_1^h becomes homogeneous in the x_2 direction.

3 Solvability of certain linear systems with measure valued sources

To prove Theorem 1 we will use two lemmas concerning solvability of linear elliptic boundary value problems with low regularity data.

Lemma 1. Assume that $0 \leq a_0 \in L_\infty(\Omega)$, $0 \leq a_{11} \in L_\infty(\partial_1\Omega)$. Then for every $h \in (0, 1]$, $\lambda > 0$ and $\mu_\Omega \in \mathcal{M}(\Omega)$, $\mu_I \in \mathcal{M}(I)$ the following boundary value problem

$$\operatorname{div}(J_h(u)) + (\lambda + a_0)u = \mu_\Omega, \quad x \in \Omega \quad (10a)$$

$$-J_h(u)\nu = 0, \quad x \in \partial_0\Omega \quad (10b)$$

$$-J_h(u)\nu + a_{11}u = \mu_I, \quad x \in \partial_1\Omega \quad (10c)$$

has a unique W_1^1 solution i.e. there exists a unique $u \in W_1^1(\Omega)$ such that for every $v \in W_\infty^1(\Omega)$

$$\int_{\Omega} [-J_h(u)\nabla v + (\lambda + a_0)uv] + \int_{\partial_1\Omega} a_{11}uv = \int_{\Omega} v d\mu_\Omega + \int_{\partial_1\Omega} v d\mu_I. \quad (11)$$

Moreover $u \in W_p^1(\Omega)$ for every $p < 2$ and

$$\|u\|_{W_p^1(\Omega)} + h^{-1}\|\partial_{x_2}u\|_{L_p(\Omega)} \leq C(\|\mu_\Omega\|_{TV} + \|\mu_I\|_{TV}), \quad (12)$$

where C depends only on $p, \lambda, \|a_0\|_{L_\infty(\Omega)}, \|a_{11}\|_{L_\infty(\partial_1\Omega)}$. If $\mu_\Omega, \mu_I \geq 0$ then $u \geq 0$.

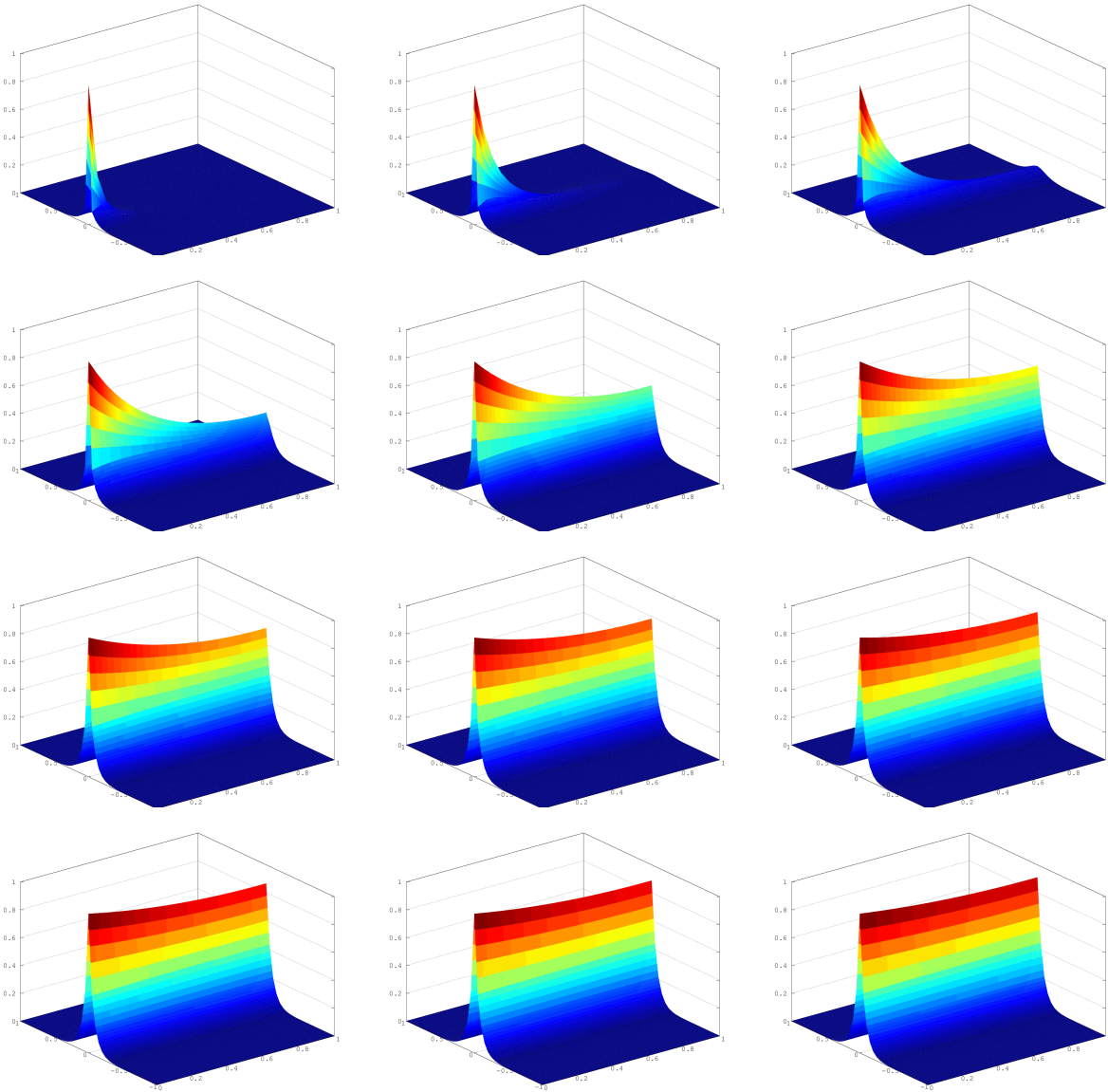


Figure 1: Graph of u_1^h , (normalised to 1) computed for the following values of parameters: $\mathbf{b} = [100, 10, 10, 10, 10]$, $\mathbf{c} = [10, 10, 1, 10, 10]$, $\mathbf{p} = [100, 0, 100, 0, 0]$, $d = 1/10$. First row - $h \in \{1, 1/3, 1/5\}$, second row - $h \in \{1/10, 1/15, 1/20\}$, third row - $h \in \{1/25, 1/30, 1/35\}$, fourth row - $h \in \{1/40, 1/45, 1/50\}$. A numerical scheme based on the finite difference method was implemented using the software Octave.

Proof. We divide the proof into two parts. In the first part we employ the technique from [1] to prove existence of the solution which additionally satisfies (12). Notice that one has to use a slight modification due to the Robin boundary condition instead of the Dirichlet condition which is treated in [1]. In the second part of the proof, using duality technique from [2], we show that the solution is unique in the W_1^1 class.

Existence

Observe that due to linearity of the problem (10) one can assume without loss of generality that

$$\|\mu_\Omega\|_{TV} + \|\mu_I\|_{TV} \leq 1.$$

First let us consider $\mu_\Omega \in L_\infty(\Omega), \mu_I \in L_\infty(\partial_1\Omega)$. Using the Lax-Milgram lemma we obtain that the problem (10) has a unique solution $u \in W_2^1(\Omega)$. We will now prove that this solution satisfies (12). Observe that if $\phi \in W_\infty^1(\mathbb{R})$ is such that

$$\|\phi\|_{L_\infty(\mathbb{R})} \leq 1, \quad y\phi(y) \geq 0, \quad \phi'(y) \geq 0, \quad (13)$$

then testing (??) by $v = \phi(u) \in W_2^1(\Omega)$ we obtain

$$\lambda \int_\Omega u\phi(u) \leq 1, \quad (14a)$$

$$0 \leq \int_\Omega -\phi'(u)J_h(u)\nabla u \leq 1. \quad (14b)$$

For $n \geq 1$ define

$$\varphi_n(y) = \begin{cases} ny & \text{if } |y| < 1/n \\ \text{sgn}(y) & \text{if } |y| \geq 1/n \end{cases}. \quad (15)$$

Choosing in (14a) $\phi = \varphi_n$ and taking $n \rightarrow \infty$ we obtain that

$$\|u\|_{L_1(\Omega)} \leq 1/\lambda \leq C. \quad (16)$$

For $n \geq 0$ define $B_n = \{x : n \leq |u(x)| \leq n+1\}$ and

$$\psi_n(y) = \begin{cases} 0 & \text{if } |y| < n \\ y - \text{sgn}(y) \cdot n & \text{if } n \leq |y| \leq n+1 \\ \text{sgn}(y) & \text{if } |y| > n+1 \end{cases}.$$

Choosing in (14b) $\phi = \psi_n$ we obtain that

$$\|m_h(u)\mathbf{1}_{B_n}\|_{L_2(\Omega)}^2 = \int_{B_n} -J_h(u)\nabla u \leq 1, \quad (17)$$

where $m_h(u) = \sqrt{|\partial_{x_1}u|^2 + h^{-2}|\partial_{x_2}u|^2}$. Using Hölder's inequality with $1 = p/2 + p/p^*$ we have

$$\|m_h(u)\mathbf{1}_{B_n}\|_{L_p(\Omega)}^p \leq \|m_h(u)\mathbf{1}_{B_n}\|_{L_2(\Omega)}^p |B_n|^{p/p^*} \leq |B_n|^{p/p^*} \leq C. \quad (18)$$

Using Sobolev's inequality and (16) we have

$$\|u\|_{L_{p^*}(\Omega)} \leq C(\|m_1(u)\|_{L_p(\Omega)} + \|u\|_{L_1(\Omega)}) \leq C(\|m_h(u)\|_{L_p(\Omega)} + 1). \quad (19)$$

From (18), Hölder inequality (for series) and (19) we have

$$\begin{aligned} \|m_h(u)\|_{L_p(\Omega)}^p &= \sum_{n=0}^N \|m_h(u)\mathbf{1}_{B_n}\|_{L_p(\Omega)}^p + \sum_{n=N+1}^{\infty} \|m_h(u)\mathbf{1}_{B_n}\|_{L_p(\Omega)}^p \leq C(N+1) + \sum_{n=N+1}^{\infty} |B_n|^{p/p^*} \\ &\leq C(N+1) + \sum_{n=N+1}^{\infty} n^{-p} \|u\mathbf{1}_{B_n}\|_{L_{p^*}(\Omega)}^p \leq C(N+1) + \left(\sum_{n=N+1}^{\infty} n^{-2} \right)^{p/2} \|u\|_{L_{p^*}(\Omega)}^p \\ &= C(N+1) + A(N)^p \|u\|_{L_{p^*}(\Omega)}^p \leq C(N+1) + CA(N)^p (\|m_h(u)\|_{L_p(\Omega)}^p + 1). \end{aligned}$$

Taking N sufficiently large we obtain

$$\|m_h(u)\|_{L_p(\Omega)} \leq C.$$

Finally from (19) it follows that $\|u\|_{L_p(\Omega)} \leq C\|u\|_{L_{p^*}(\Omega)} \leq C(\|m_h(u)\|_{L_p(\Omega)} + 1) \leq C$ which completes the proof of (12).

The case of arbitrary Radon measures μ_Ω, μ_I follows by standard approximation, see [1] for instance.

Uniqueness

We shall use duality technique. Let u be a W_1^1 solution to

$$\operatorname{div}(J_h(u)) + (\lambda + a_0)u = 0, \quad x \in \Omega \quad (20a)$$

$$-J_h(u)\nu = 0, \quad x \in \partial_0\Omega \quad (20b)$$

$$-J_h(u)\nu + a_{11}u = 0, \quad x \in \partial_1\Omega. \quad (20c)$$

We intend to prove that $u \equiv 0$. First we assume additionally that $a_{11} \equiv 0$. Using [3] we get that for every $f \in L_q(\Omega), q > 2$, problem

$$\operatorname{div}(J_h(v)) + (\lambda + a_0)v = f, \quad x \in \Omega \quad (21a)$$

$$-J_h(v)\nu = 0, \quad x \in \partial\Omega \quad (21b)$$

has a unique solution $v \in W_q^2(\Omega)$. Since $q > 2$ we have $W_q^2(\Omega) \subset W_\infty^1(\Omega)$, so that for every $w \in W_1^1(\Omega)$ we have

$$\int_\Omega [-J_h(v)\nabla w + (\lambda + a_0)vw] = \int_\Omega fw.$$

Taking $w = u$ we thus get $\int_\Omega fu = 0$ and since f was arbitrary - $u \equiv 0$ follows.

Now let us take $0 \leq a_{11} \in L_\infty(\partial_1\Omega)$. Denote $g = -a_{11}u$. Observe that u is a W_1^1 solution of

$$\operatorname{div}(J_h(u)) + (\lambda + a_0)u = 0, \quad x \in \Omega \quad (22a)$$

$$-J_h(u)\nu = 0, \quad x \in \partial_0\Omega \quad (22b)$$

$$-J_h(u)\nu = g, \quad x \in \partial_1\Omega. \quad (22c)$$

As we already showed (22) has a unique W_1^1 solution and, thus $u \in W_p^1(\Omega)$ for every $p < 2$. In particular $g \in L_q(\partial_1\Omega)$ for every $q < \infty$. We can now use Lax-Milgram theorem to prove that (22) has a unique W_2^1 solution and thus conclude that $u \in W_2^1(\Omega)$. It follows that, u is also a W_2^1 solution of (20), whence $u \equiv 0$. □

Lemma 2. *Assume that $d > 0$, $0 \leq a_0 \in L_\infty(\Omega)$ and*

$$a_{ij} \in L_\infty(\partial_1\Omega), \quad a_{11} \geq |a_{21}|, a_{22} \geq |a_{12}|. \quad (23)$$

Then for every $h \in (0, 1], \lambda > 0, \mu_\Omega \in \mathcal{M}(\Omega), \mu_I \in \mathcal{M}(I)$ the following system

$$\operatorname{div}(J_h(u_1)) + (\lambda + a_0)u_1 = \mu_\Omega, \quad x \in \Omega \quad (24a)$$

$$-d\partial_{x_1}^2 u_2 - a_{21}u_1 + (\lambda + a_{22})u_2 = 0, \quad x \in \partial_1\Omega \quad (24b)$$

with boundary conditions

$$-J_h(u_1)\nu = 0, \quad x \in \partial_0\Omega \quad (25a)$$

$$-J_h(u_1)\nu + a_{11}u_1 - a_{12}u_2 = \mu_I, \quad x \in \partial_1\Omega \quad (25b)$$

$$\partial_{x_1} u_2 = 0, \quad x \in \partial\partial_1\Omega, \quad (25c)$$

has a unique W_1^1 solution i.e. there exists a unique $(u_1, u_2) \in W_1^1(\Omega) \times W_1^1(\partial_1\Omega)$ such that for every $(v_1, v_2) \in W_\infty^1(\Omega) \times W_\infty^1(\partial_1\Omega)$:

$$\begin{aligned} \int_{\Omega} [-J_h(u_1)\nabla v_1 + (\lambda + a_0)u_1v_1] + \int_{\partial_1\Omega} \left[d\partial_{x_1}u_2\partial_{x_1}v_2 + \lambda u_2v_2 - \left(M(u_1, u_2) \middle| (v_1, v_2) \right)_{\mathbb{R}^2} \right] \\ = \int_{\Omega} v_1 d\mu_{\Omega} + \int_{\partial_1\Omega} v_1 d\mu_I, \end{aligned}$$

where $M(u_1, u_2) = (-a_{11}u_1 + a_{12}u_2, a_{21}u_1 - a_{22}u_2)$.

Moreover $(u_1, u_2) \in W_p^1(\Omega) \times W_q^2(\partial_1\Omega)$ for every $1 \leq p < 2, 1 \leq q < \infty$ and

$$\|u_1\|_{W_p^1(\Omega)} + h^{-1}\|\partial_{x_2}u_1\|_{L_p(\Omega)} + \|u_2\|_{W_q^2(\partial_1\Omega)} \leq C(\|\mu_{\Omega}\|_{TV} + \|\mu_I\|_{TV}), \quad (26)$$

where C depends only on $p, \lambda, d, \|a_0\|_{L_\infty(\Omega)}, \|a_{ij}\|_{L_\infty(\partial_1\Omega)}$. If $\mu_{\Omega}, \mu_I, a_{12}, a_{21} \geq 0$ then $u_1, u_2 \geq 0$.

Proof. Existence

Let us define the Hilbert spaces $X_{1/2} = W_2^1(\Omega) \times W_2^1(\partial_1\Omega)$, $X_{-1/2} = X_{1/2}^*$ and an unbounded operator $A : X_{-1/2} \supset X_{1/2} \rightarrow X_{-1/2}$ by

$$\left\langle A(u_1, u_2), (v_1, v_2) \right\rangle_{(X_{-1/2}, X_{1/2})} = \int_{\Omega} [J_h(u_1)\nabla v_1 - a_0u_1v_1] + \int_{\partial_1\Omega} \left[-d\partial_{x_1}u_2\partial_{x_1}v_2 + \left(M(u_1, u_2) \middle| (v_1, v_2) \right)_{\mathbb{R}^2} \right].$$

Due to boundedness of a_0 and a_{ij} operator $\lambda - A$ is coercive for λ large enough and the Lax-Milgram lemma guarantees that there is $\lambda_0 > 0$ such that $[\lambda_0, \infty) \subset \rho(A)$ ($\rho(A)$ denotes the resolvent set of A). Because $X_{1/2}$ is compactly embedded into $X_{-1/2}$ we get that for $\lambda \in \rho(A)$ the resolvent operator $(\lambda - A)^{-1}$ is compact and thus the spectrum $\sigma(A)$ consists entirely of eigenvalues. Choose any $\lambda \in \mathbb{R}$, $\theta \in X_{-1/2}$ and $u = (u_1, u_2) \in X_{1/2}$ such that $(\lambda - A)u = \theta$. Let φ_n be the function defined in (15). Then

$$\begin{aligned} \left\langle \theta, (\varphi_n(u_1), \varphi_n(u_2)) \right\rangle_{(X_{-1/2}, X_{1/2})} &= \left\langle (\lambda - A)(u_1, u_2), (\varphi_n(u_1), \varphi_n(u_2)) \right\rangle_{(X_{-1/2}, X_{1/2})} \\ &= \int_{\Omega} [-\varphi_n'(u_1)J_h(u_1)\nabla u_1 + (\lambda + a_0)u_1\varphi_n(u_1)] \\ &\quad + \int_{\partial_1\Omega} \left[d\varphi_n'(u_2)|\partial_{x_1}u_2|^2 - \left(M(u_1, u_2) \middle| (\varphi_n(u_1), \varphi_n(u_2)) \right)_{\mathbb{R}^2} + \lambda u_2\varphi_n(u_2) \right] \\ &\geq \lambda \left(\int_{\Omega} u_1\varphi_n(u_1) + \int_{\partial_1\Omega} u_2\varphi_n(u_2) \right) - \int_{\Omega} \left(M(u_1, u_2) \middle| (\varphi_n(u_1), \varphi_n(u_2)) \right)_{\mathbb{R}^2}. \end{aligned}$$

Thus taking $n \rightarrow \infty$ and using (23) we get

$$\liminf_{n \rightarrow \infty} \left\langle \theta, (\varphi_n(u_1), \varphi_n(u_2)) \right\rangle_{(X_{-1/2}, X_{1/2})} \geq \lambda(\|u_1\|_{L_1(\Omega)} + \|u_2\|_{L_1(\partial_1\Omega)}). \quad (27)$$

In particular it follows from (27) that for $\lambda > 0$ equation $(\lambda - A)u = 0$ does not have nontrivial solutions, whence $(0, \infty) \subset \rho(A)$.

Observe that when μ_{Ω}, μ_I are bounded functions then the distribution θ defined by

$$\left\langle \theta, (v_1, v_2) \right\rangle = \int_{\Omega} v_1 d\mu_{\Omega} + \int_I v_1 d\mu_I = \int_{\Omega} v_1 \mu_{\Omega} dx + \int_I v_1(\cdot, 0) \mu_I dx_1 \quad (28)$$

belongs to $X_{1/2}^*$ thus equation $(\lambda - A)u = \theta$ has a unique solution $u = (u_1, u_2) \in X_{1/2}$ which is a solution to problem (24)-(25). We will now prove that u satisfies (26). Due to linearity of (24), (25) we can assume, without loss of generality, that

$$\|\mu_{\Omega}\|_{TV} + \|\mu_I\|_{TV} \leq 1.$$

Next we prove respectively that

$$\lambda(\|u_1\|_{L_1(\Omega)} + \|u_2\|_{L_1(\partial_1\Omega)}) \leq C, \quad (29)$$

$$\|u_1\|_{W_p^1(\Omega)} + h^{-1}\|\partial_{x_2}u_1\|_{L_p(\partial_1\Omega)} \leq C, \quad (30)$$

$$\|u_2\|_{W_q^2(\partial_1\Omega)} \leq C. \quad (31)$$

To get (29) observe that from (27) with θ given by (28) one has

$$\lambda(\|u_1\|_{L_1(\Omega)} + \|u_2\|_{L_1(\partial_1\Omega)}) \leq \liminf_{n \rightarrow \infty} \left\langle \theta, (\varphi_n(u_1), \varphi_n(u_2)) \right\rangle_{(X_{-1/2}, X_{1/2})} \leq \|\mu_\Omega\|_{L_1(\Omega)} + \|\mu_I\|_{L_1(I)} \leq 1,$$

since $|\varphi_n(y)| \leq 1$ for $y \in \mathbb{R}$. Then (30) follows from (29) and Lemma 1, while (31) follows from (24b), (30) and the fact that for every $1 \leq q < \infty$ there exists $1 \leq p < 2$ such that the trace operator maps $W_p^1(\Omega)$ into $L_q(\partial_1\Omega)$. To prove existence of solutions to (24), (25) for the case when μ_Ω and μ_I are finite Radon measures one proceeds by the standard approximation technique with the use of (26).

Uniqueness

Let (u_1, u_2) be a W_1^1 solution of problem (24), (25) with $\lambda > 0, \mu_\Omega = 0, \mu_I = 0$.

Denoting $g_1 = a_{12}u_2 \in L_\infty(I), g_2 = a_{21}u_1 \in L_1(I)$ we see that u_1 is a W_1^1 solution of

$$\operatorname{div}(J_h(u)) + (\lambda + a_0)u = 0, \quad x \in \Omega \quad (32a)$$

$$-J_h(u)\nu = 0, \quad x \in \partial_0\Omega \quad (32b)$$

$$-J_h(u)\nu + a_{11}u = g_1, \quad x \in \partial_1\Omega \quad (32c)$$

and u_2 is a W_1^1 solution of

$$-d\partial_{x_1}^2 u + (\lambda + a_{22})u = g_2, \quad x \in I \quad (33a)$$

$$\partial_{x_1}u = 0, \quad x \in \partial I. \quad (33b)$$

Since $g_1 \in L_\infty(\partial_1\Omega)$ then by Lax-Milgram lemma problem (32) has a W_2^1 solution which by Lemma 1 is unique in W_1^1 class. Thus u_1 is a W_2^1 solution of (32) and $g_2 \in L_2(I)$. From Lax-Milgram lemma we obtain that (33) has a W_2^1 solution which due to duality technique is unique in W_1^1 class. Thus $u_2 \in W_2^1$. Finally we observe that $(u_1, u_2) \in X_{1/2}$ is in the kernel of the operator $(\lambda - A)$ and thus $(u_1, u_2) \equiv 0$. \square

4 Proof of Theorem 1

Existence

Fix $1 > s > 1/p, \infty > q > 1$ and for $R > 0$ define

$$K_R = \{(v_1, v_2) \in W_p^s(\Omega) \times L_q(\partial_1\Omega) : v_1, v_2 \geq 0, \|v_1\|_{W_p^s(\Omega)} + \|v_2\|_{L_q(\partial_1\Omega)} \leq R\}.$$

K_R is a bounded, convex and closed subset of the Banach space $B = W_p^s(\Omega) \times L_q(\partial_1\Omega)$. For $(v_1, v_2) \in K_R$ consider problem (3)-(4) with $H(u_1, u_2)$ replaced by $H(v_1, v_2)$ (notice that $v_1(0, \cdot)$ is well defined as $s > 1/p$) i.e.

$$\operatorname{div}(J_h(u_1)) + b_1u_1 = 0, \quad x \in \Omega \quad (34a)$$

$$-d\partial_{x_1}^2 u_2 - c_1u_1 + (b_2 + c_2 + k_2H(v_1, v_2))u_2 = 0, \quad x \in \partial_1\Omega \quad (34b)$$

with boundary conditions

$$-J_h(u_1)\nu = 0, \quad x \in \partial_0\Omega \quad (35a)$$

$$-J_h(u_1)\nu = -(c_1 + k_1H(v_1, v_2))u_1 + c_2u_2 + p_1\delta, \quad x \in \partial_1\Omega \quad (35b)$$

$$\partial_{x_1}u_2 = 0, \quad x \in \partial\partial_1\Omega. \quad (35c)$$

Using Lemma 2 with

$$\begin{aligned} \lambda &= \min\{b_1, b_2\}, \quad a_0 = b_1 - \lambda, \quad \mu_\Omega = 0, \quad \mu_I = p_1\delta, \\ a_{11} &= c_1 + k_1 H(v_1, v_2), & a_{12} &= c_2, \\ a_{21} &= c_1, & a_{22} &= b_2 - \lambda + c_2 + k_2 H(v_1, v_2), \end{aligned}$$

we obtain that problem (34) has the unique solution $(u_1, u_2) = T(v_1, v_2)$ satisfying (26) with C independent of R (since H is bounded on \mathbb{R}_+^2). Thus for large R the nonlinear operator T maps K_R into itself. Since $W_p^1(\Omega) \times W_q^2(\partial_1\Omega)$ embeds compactly into $W_p^s(\Omega) \times L_q(\partial_1\Omega)$ the nonlinear operator T is compact. Since H is globally Lipschitz we conclude that T is continuous in the topology of B . Thus, using Schauder fixed point theorem, T has a fixed point, which additionally satisfies (7).

Uniqueness

Assume that $(u_1, u_2), (v_1, v_2)$ are two W_1^1 solutions of (3)-(4). Denoting $z_i = u_i - v_i$ for $i = 1, 2$ we have:

$$\begin{aligned} \operatorname{div}(J_h(z_1)) + b_1 z_1 &= 0, & x &\in \Omega \\ -d\partial_{x_1}^2 z_2 - c_1 z_1 + (b_2 + c_2)z_2 + k_2(H(u_1, u_2)u_2 - H(v_1, v_2)v_2) &= 0, & x &\in \partial_1\Omega \end{aligned}$$

with boundary conditions

$$\begin{aligned} -J_h(z_1)\nu &= 0, & x &\in \partial_0\Omega \\ -J_h(z_1)\nu &= -c_1 z_1 - k_1(H(u_1, u_2)u_1 - H(v_1, v_2)v_1) + c_2 z_2, & x &\in \partial_1\Omega \\ \partial_{x_1} z_2 &= 0, & x &\in \partial\partial_1\Omega. \end{aligned}$$

Define

$$\begin{aligned} D &= (k_1 u_1 + k_2 u_2 + b_3)(k_1 v_1 + k_2 v_2 + b_3), \\ w_i &= (u_i + v_i)/2, \quad i = 1, 2. \end{aligned}$$

Notice that

$$\begin{aligned} u_1 v_2 - u_2 v_1 &= z_1(u_2 + v_2)/2 - z_2(u_1 + v_1)/2 = z_1 w_2 - z_2 w_1, \\ H(u_1, u_2)u_1 - H(v_1, v_2)v_1 &= p_3 \left(\frac{u_1}{k_1 u_1 + k_2 u_2 + b_3} - \frac{v_1}{k_1 v_1 + k_2 v_2 + b_3} \right) = \frac{p_3}{D} (k_2(u_1 v_2 - u_2 v_1) + b_3 z_1) \\ &= \frac{p_3}{D} ((k_2 w_2 + b_3)z_1 - k_2 w_1 z_2), \\ H(u_1, u_2)u_2 - H(v_1, v_2)v_2 &= p_3 \left(\frac{u_2}{k_1 u_1 + k_2 u_2 + b_3} - \frac{v_2}{k_1 v_1 + k_2 v_2 + b_3} \right) = \frac{p_3}{D} (-k_1(u_1 v_2 - u_2 v_1) + b_3 z_2) \\ &= \frac{p_3}{D} (-k_1 w_2 z_1 + (k_1 w_1 + b_3)z_2). \end{aligned}$$

Thus

$$\begin{aligned} \operatorname{div}(J_h(z_1)) + b_1 z_1 &= 0, & x &\in \Omega \\ -d\partial_{x_1}^2 z_2 - (c_1 + \frac{k_1 k_2 p_3 w_2}{D})z_1 + (b_2 + \frac{k_2 p_3 b_3}{D} + c_2 + \frac{k_1 k_2 p_3 w_1}{D})z_2 &= 0, & x &\in \partial_1\Omega \end{aligned}$$

with boundary conditions

$$\begin{aligned} -J_h(z_1)\nu &= 0, & x &\in \partial_0\Omega \\ -J_h(z_1)\nu + (\frac{k_1 p_3 b_3}{D} + c_1 + \frac{k_1 k_2 p_3 w_2}{D})z_1 - (c_2 + \frac{k_1 k_2 p_3 w_1}{D})z_2 &= 0, & x &\in \partial_1\Omega \\ \partial_{x_1} z_2 &= 0, & x &\in \partial\partial_1\Omega. \end{aligned}$$

Hence, using the notation introduced in Lemma 2, (z_1, z_2) is a W_1^1 solution of (24),(25) with

$$\begin{aligned} \lambda &= \min\{b_1, b_2\}, \quad a_0 = b_1 - \lambda, \quad \mu_\Omega = 0, \quad \mu_I = 0 \\ a_{11} &= \frac{k_1 p_3 b_3}{D} + c_1 + \frac{k_1 k_2 p_3 w_2}{D}, & a_{12} &= c_2 + \frac{k_1 k_2 p_3 w_1}{D}, \\ a_{21} &= c_1 + \frac{k_1 k_2 p_3 w_2}{D}, & a_{22} &= b_2 - \lambda + \frac{k_2 p_3 b_3}{D} + c_2 + \frac{k_1 k_2 p_3 w_1}{D}. \end{aligned}$$

Since the nonnegativity of w_1, w_2 ensures that assumption (23) is fulfilled we infer that $z_1 = z_2 = 0$.

5 Proof of Theorem 2

Since the spaces $W_p^1(\Omega)$ and $W_q^2(\partial_1\Omega)$ are reflexive for $1 < p < 2$, $1 < q < \infty$ thus, owing to (7), there exists a sequence $(h_k)_{k=1}^\infty \subset (0, 1]$ such that $\lim_{k \rightarrow \infty} h_k = 0$ and

$$u_1^{h_k} \rightharpoonup w_1 \quad \text{in } W_p^1(\Omega), \quad (36a)$$

$$u_2^{h_k} \rightharpoonup w_2 \quad \text{in } W_q^2(\partial_1\Omega). \quad (36b)$$

Now we claim that

$$\partial_{x_2} w_1 \equiv 0, \quad (37a)$$

$$u_1^{h_k}(0, \cdot) \rightarrow w_1(0, \cdot) \quad \text{in } L_q(\partial_1\Omega), \quad (37b)$$

$$u_2^{h_k} \rightarrow w_2 \quad \text{in } C(\bar{\Gamma}). \quad (37c)$$

Indeed (37a) comes from (7). To prove (37b) fix any $1 < q < \infty$, then choose s, p such that $1 < p < 2, 1/p < s < 1, s - 2/p \geq -1/q$. Then $W_p^1(\Omega)$ embeds compactly into $W_p^s(\Omega)$, the trace operator maps $W_p^s(\Omega)$ into $W_p^{s-1/p}(\partial_1\Omega)$ and the latter space embeds continuously into $L_q(\partial_1\Omega)$. Finally (37c) follows from compact embedding of $W_q^2(\partial_1\Omega)$ into $C(\bar{\partial_1\Omega})$. Choose $v_1 \in C^1(\bar{\Omega})$, $v_2 \in C^1(\bar{\partial_1\Omega})$, then by (6)

$$\begin{aligned} \int_\Omega [\partial_{x_1} u_1^{h_k} \partial_{x_1} v_1 + b_1 u_1^{h_k} v_1] + \int_{\partial_1\Omega} [d \partial_{x_1} u_2^{h_k} \partial_{x_1} v_2 - c_1 u_1^{h_k} v_2] &= p_1 v_1(0), \\ \int_{\partial_1\Omega} [c_1 H(u_1^{h_k}, u_2^{h_k}) u_1^{h_k} v_1 - c_2 u_2^{h_k} v_1 + (b_2 + c_2) H(u_1^{h_k}, u_2^{h_k}) v_2] &= 0. \end{aligned}$$

Using (36) and (37) we can pass to the limit with $k \rightarrow \infty$ and identify that $(w_1, w_2) = (u_1^0, u_2^0)$ is a solution of (9). Finally notice that (8) follows from (36) and the fact that (??) has a unique solution, as was proved in [11].

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