

## Research Article

# An Existence Result to a Strongly Coupled Degenerated System Arising in Tumor Modeling

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We consider a mathematical model to describe the growth of a vascular tumor including tumor cells, macrophages, and blood vessels. The resulting system of equations is reduced to a strongly  $2 \times 2$  coupled nonlinear parabolic system of degenerate type. Assuming the initial data are far enough from 0, we prove existence of a global weak solution with finite entropy to the problem by using an approximation procedure and a time discrete scheme.

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## 1. Introduction

The theory of mixtures is used to develop a mathematical model that governs the interactions of macrophages, tumor cells, and blood vessels within a vascular tumor, focusing on the ability of macrophages to both lyse tumor cells and stimulate angiogenesis. In recent years, a variety of macroscopic continuum models have been derived by [1–6]. In their wake, we present hereafter a simplified model.

The vascular tumor is viewed as a mixture of three constituents: tumor cells, tumor-associated macrophages (abbreviated by TAMs), and blood vessels. We denote their respective volume fractions by  $\alpha$ ,  $\beta$ , and  $\gamma$ , and we assume that the mixture is saturated, so we take

$$\alpha + \beta + \gamma = 1. \quad (1.1)$$

We suppose that the tumor undergoes one dimensional and one side growth, parallel to the  $x$ -axis, by occupying the region  $0 \leq x \leq L(t)$ . Each phase is associated with velocity, pressure, and spatial stress denoted, respectively, by  $v_1$ ,  $P_1$ ,  $\sigma_1$  for the tumor cells,  $v_2$ ,  $P_2$ ,  $\sigma_2$  for the

TAMs and  $v_3$ ,  $P_3$ ,  $\sigma_3$  for the blood vessels. Formulating conservation of mass for the three volume fractions, under the assumption that each phase has the same constant density, we get

$$\alpha_t + (\alpha v_1)_x = q_1, \quad \beta_t + (\beta v_2)_x = q_2, \quad \gamma_t + (\gamma v_3)_x = q_3, \quad (1.2)$$

where the indices  $t$  and  $x$  are set for partial derivatives and  $q_1$ ,  $q_2$ , and  $q_3$  are the rates of production related to each phase, satisfying  $q_1 + q_2 + q_3 = 0$ . We suppose that the volume fraction of tumor cells increase by proliferation and decrease by apoptosis, necrosis or lysis, the volume fraction of TAMs increase by proliferation and by influx from capillaries and decrease by natural death or after lysing tumor cells. Thus, we write

$$q_1(\alpha, \beta, \gamma) = k_1\alpha\gamma - k_2\alpha - k_3(1 - \gamma)\alpha - k_4\alpha\beta, \quad (1.3)$$

$$q_2(\alpha, \beta, \gamma) = k_5\beta(1 - \sigma(\alpha + \gamma)) - k_6\beta(1 - \alpha) - k_7\alpha\beta, \quad (1.4)$$

where  $\sigma$  and  $k_i$ ,  $i = 1, \dots, 7$  are nonnegative constants. Assuming that the momentum is conserved and the motions of cells and blood vessels are so slow that inertial terms can be neglected, we can write

$$(\alpha\sigma_1)_x + F_1 = 0, \quad (\beta\sigma_2)_x + F_2 = 0, \quad (\gamma\sigma_3)_x + F_3 = 0, \quad (1.5)$$

where

$$F_1 = P\alpha_x + d\alpha\beta(v_2 - v_1) + d\alpha\gamma(v_3 - v_1), \quad (1.6)$$

$$F_2 = P\beta_x - d\alpha\beta(v_2 - v_1) + d\beta\gamma(v_3 - v_2), \quad (1.7)$$

$$F_3 = P\gamma_x - d\alpha\gamma(v_3 - v_1) - d\beta\gamma(v_3 - v_2), \quad (1.8)$$

represent the momentum supply related to each phase,  $d$  is a positive constant and  $P$  is assumed to be a common pressure. When neglecting viscous effect, the partial stress tensors are given by

$$\sigma_i = -P_i = -(P + \Sigma_i), \quad i = 1, 2, 3, \quad (1.9)$$

where

$$\Sigma_1 = \lambda\alpha, \quad \Sigma_2 = \mu\beta(1 + \theta\alpha), \quad \Sigma_3 = P_0 \quad (1.10)$$

represent the pressures due to cell-cell interactions exerted on tumor cells, macrophages and blood vessels respectively.  $\lambda$ ,  $\mu$  and  $\theta$  are nonnegative constants and  $P_0 > 0$  is constant.

The following initial and boundary conditions are considered:

$$L = l > 0, \quad \alpha = \alpha_0 \geq 0, \quad \beta = \beta_0 \geq 0, \quad \alpha_0 + \beta_0 \leq 1 \quad \text{at } t = 0, \quad (1.11)$$

$$\alpha = \alpha_b \geq 0, \quad \beta = \beta_b \geq 0, \quad \alpha_b + \beta_b \leq 1 \quad \text{at } x = 0. \quad (1.12)$$

We impose the no flux boundary condition at the free boundary that we suppose moving at the same velocity as the tumor cells, so

$$v_1 = v_2 = v_3 = 0 \quad \text{at } x = L(t), \quad (1.13)$$

$$\frac{dL}{dt} = v_1 \Big|_{x=L(t)} = 0 \quad \text{that is } L(t) = l \quad \forall t \geq 0. \quad (1.14)$$

Adding the three continuity equations (1.2) and the three momentum equations (1.5), we get using (1.13)

$$\alpha v_1 + \beta v_2 + \gamma v_3 = 0, \quad (\alpha \Sigma_1)_x + (\beta \Sigma_2)_x + (\gamma \Sigma_3)_x = 0. \quad (1.15)$$

The last equality and (1.9) imply

$$P_x = -(\alpha \Sigma_1 + \beta \Sigma_2 + \gamma \Sigma_3)_x. \quad (1.16)$$

Using (1.6), (1.9), and the first relation in (1.15), the first equation of (1.5) reduces to give either  $\alpha = 0$ , which we reject because it can be only transient, or

$$P_x + \frac{1}{\alpha} (\alpha \Sigma_1)_x = -d v_1, \quad (1.17)$$

which together with (1.16) gives

$$v_1 = \frac{1}{d} \left( (\alpha \Sigma_1 + \beta \Sigma_2 + \gamma \Sigma_3)_x - \frac{1}{\alpha} (\alpha \Sigma_1)_x \right). \quad (1.18)$$

Using (1.10) and the fact that  $P_0$  is constant, (1.18) can be rewritten as follows:

$$v_1 = \frac{1}{d} (\alpha_x (2\lambda\alpha + \mu\theta\beta^2 - P_0 - 2\lambda) + \beta_x (2\mu\beta(1 + \theta\alpha) - P_0)). \quad (1.19)$$

Similarly, the second equation of (1.5) simplifies into

$$v_2 = \frac{1}{d} (\alpha_x (2\lambda\alpha + \mu\theta\beta^2 - P_0 - \mu\theta\beta) + \beta_x (2\mu(\beta - 1)(1 + \theta\alpha) - P_0)). \quad (1.20)$$

Thus, substituting the relations (1.19)-(1.20) into (1.2), the equations of  $\alpha$  and  $\beta$  become

$$\begin{aligned} \alpha_t - \frac{1}{d} ((2\lambda\alpha(1 - \alpha) - \mu\theta\alpha\beta^2 + P_0\alpha)\alpha_x + (-2\mu\beta\alpha(1 + \theta\alpha) + P_0\alpha)\beta_x) &= q_1, \\ \beta_t - \frac{1}{d} ((-2\lambda\alpha\beta + \mu\theta\beta^2(1 - \beta) + P_0\beta)\alpha_x + (2\mu\beta(1 - \beta)(1 + \theta\alpha) + P_0\beta)\beta_x) &= q_2. \end{aligned} \quad (1.21)$$

Having regard to the saturation condition (1.1), we omit the equation of  $\gamma$ . The resulting problem (1.21) is strongly coupled with full diffusion matrix which is generally not positive definite. To simplify it, we reduce the number of biological parameters by setting

$$\lambda = \mu = P_0, \quad \theta = 0. \quad (1.22)$$

In this case, (1.13), (1.14), (1.19) and (1.20) reduce the boundary condition at  $x = l$  to

$$\alpha_x = \beta_x = 0. \quad (1.23)$$

Without loss of generality, we set  $l = 1$ ,  $2\lambda/d = 1$  and for technical reasons, to get the maximum principle (see Lemma 3.7), we need to take  $\sigma = 1$  in (1.4) and

$$k_5 \leq k_6. \quad (1.24)$$

In summary, denoting  $u = (\alpha, \beta)$ ,  $u_0 = (\alpha_0, \beta_0)$ ,  $u_b = (\alpha_b, \beta_b)$  and  $q = (q_1, q_2)$ , the problem (1.21) simplifies into

$$u_t - (A(u)u_x)_x = q(u), \quad (1.25)$$

with  $A$  and  $q$  given by

$$A(\alpha, \beta) = \begin{pmatrix} \alpha \left( \frac{3}{2} - \alpha \right) & \alpha \left( \frac{1}{2} - \beta \right) \\ \beta \left( \frac{1}{2} - \alpha \right) & \beta \left( \frac{3}{2} - \beta \right) \end{pmatrix}, \quad (1.26)$$

$$q_1(\alpha, \beta) = k_1\alpha(1 - \alpha - \beta) - k_2\alpha - k_3\alpha(\alpha + \beta) - k_4\alpha\beta,$$

$$q_2(\alpha, \beta) = k_5\beta^2 - k_6\beta(1 - \alpha) - k_7\alpha\beta.$$

The system (1.25) is complemented with the boundary and initial conditions

$$\begin{aligned} u(t, 0) &= u_b(t), & u_x(t, 1) &= 0, \\ u(0, x) &= u_0(x), \end{aligned} \quad (1.27)$$

and has to be solved in  $\mathbb{R}_+ \times (0, 1)$ .

In recent years, cross-diffusion systems have drawn a great deal attention. For example in [7], the global existence was established, as well as the existence of a global attractor in a case of triangular positive definite diffusion matrix. In [8], the well-posedness and the properties of steady states for a degenerate parabolic system with triangular positive (semi) definite matrix, modeling the chemotaxis movement of cells, were investigated. In [9, 10], the existence of global weak solution was shown for a nonlinear problem with full diffusion matrix. The proof was based on a symmetrization of the problem via an exponential transformation of variables, backward Euler approximation of the time derivative and

an entropy functional. Here, we use analogous arguments, but in our case, after the transformation of variables the resulting matrix  $B$  is not positive definite. To overcome this difficulty, we approximate  $B$  by positive definite matrices  $B^\tau$  which tend towards  $B$  as  $\tau \rightarrow 0$ , if the condition  $0 \leq \alpha, \beta, \alpha + \beta \leq 1$  is satisfied. This needs to prove that the set  $\{(\alpha, \beta) \in L^\infty(\Omega) \times L^\infty(\Omega), 0 \leq \alpha, \beta, \alpha + \beta \leq 1\}$  is time invariant.

Throughout this paper, we use the following notations: let  $T, \tau$  be positive real numbers, we will denote by  $C$  all the positive constants which are independent of  $\tau$ . We set  $\Omega = (0, 1)$ ,  $Q_T = (0, T) \times \Omega$  and  $s^+ = \max(s, 0)$  the positive part of the real number  $s$ . We write  $u_x := \partial_x u$  and  $u_t := \partial_t u$  for partial derivatives of a real-valued function  $u = u(t, x)$ . Moreover we will use the Sobolev space  $H_D^1(\Omega) = \{u \in H^1(\Omega); u(0) = 0\}$  equipped with the norm of  $H^1$  and we denote as usual, by  $(H^1)'$  the dual of  $H^1$ . In the case of vectorial functions, we designate the corresponding Lebesgue and Sobolev spaces, respectively, by  $\mathbb{L}^2, \mathbb{L}^\infty, \mathbb{H}^1, \mathbb{H}_D^1$ . Finally we set  $\ln(r, s) = (\ln r, \ln s)$  for  $r, s > 0$  and  $e^{(r, s)} = (e^r, e^s)$  for  $r, s \in \mathbb{R}$ .

The remainder of this paper is organized as follows. In Section 2, we introduce the weak formulation of the problem and state our main existence result in Theorem 2.2. In proving this theorem, we define and solve in Section 3 an auxiliary problem which will be useful further. Then, in Section 4, we formulate a semidiscrete version in time of the problem, using a backward Euler approximation, combined with a perturbation of the diffusion matrix. This leads to a recursive sequence of elliptic problems depending on the small parameter  $\tau$ . Performing the limit as  $\tau \rightarrow 0$ , with the help of Aubin compactness lemma and the Sobolev embedding  $H^1(0, 1) \hookrightarrow L^\infty(0, 1)$ , we get a weak solution to our problem. Finally, an appendix is devoted to the proof of a technical lemma.

## 2. Main result

We set the following assumptions:

$$(H1) \quad \alpha_0, \beta_0 \in H^1(\Omega), 0 < \alpha_0, \beta_0, \alpha_0 + \beta_0 \leq 1, \ln \alpha_0, \ln \beta_0 \in L^\infty(\Omega),$$

$$(H2) \quad \alpha_b, \beta_b \in \mathbb{R}, 0 < \alpha_b, \beta_b, \alpha_b + \beta_b \leq 1.$$

The matrix  $A(\alpha, \beta)$  is not positive even if  $0 \leq \alpha, \beta, \alpha + \beta \leq 1$ , so the problem (1.25)–(1.27) has no classical solution in general. A weak solution is defined as follows.

*Definition 2.1.* Let (H1)-(H2) be satisfied and let  $T > 0$ .  $u = (\alpha, \beta)$  is said to be a weak solution of problem (1.25)–(1.27) on  $Q_T$  if

- (1)  $u \in L^2(0, T; \mathbb{H}^1(\Omega)) \cap H^1(0, T; (\mathbb{H}^1(\Omega))') \cap \mathbb{L}^\infty(Q_T)$  with  $0 \leq \alpha, \beta, \alpha + \beta \leq 1$ ,
- (2)  $u(0, x) = u_0(x)$  a.e. in  $\Omega$ ,  $u(t, 0) = u_b$  a.e. in  $(0, T)$ ,
- (3)  $\int_0^T \langle u_t, \varphi \rangle dt + \int_{Q_T} A(u) u_x \cdot \varphi_x dx dt = \int_{Q_T} q(u) \cdot \varphi dx dt$ , for all  $\varphi \in L^2(0, T; \mathbb{H}_D^1(\Omega))$ , where  $\langle \cdot, \cdot \rangle$  is the dual product between  $(\mathbb{H}^1(\Omega))'$  and  $\mathbb{H}^1(\Omega)$ .

Our main result is the following.

**Theorem 2.2.** *Assume (H1)-(H2) are satisfied. Then for every  $T > 0$ , there exists (at least) a weak solution  $u = (\alpha, \beta)$  on  $Q_T$  to the system (1.25)–(1.27), satisfying the entropy inequality*

$$\int_{\Omega} (G_1(\alpha(t)) + G_2(\beta(t))) dx + \frac{1}{4} \int_0^t \int_{\Omega} (|\alpha_x|^2 + |\beta_x|^2) dx ds \leq \int_{\Omega} (G_1(\alpha_0) + G_2(\beta_0)) dx + C, \quad (2.1)$$

where  $C > 0$  depends on  $T, \alpha_b, \beta_b, k_i, i = 1, \dots, 7, G_1, G_2$  being positive functions defined on  $\mathbb{R}_+$  by

$$G_1(s) = s(\ln s - \ln \alpha_b - 1) + \alpha_b, \quad G_2(s) = s(\ln s - \ln \beta_b - 1) + \beta_b. \quad (2.2)$$

The proof of this existence result is based on the entropy inequality (2.1), which is formally obtained by testing (1.25) with  $(\ln(\alpha/\alpha_b), \ln(\beta/\beta_b))$ , and integrating by parts (see Section 3.3 for details).

This estimate suggests to use the change of unknown  $U = \ln(\alpha, \beta)$ , which transforms the problems (1.25)–(1.27) into the following one

$$\begin{aligned} (e^U)_t - (B(U)U_x)_x &= Q(U) \quad \text{in } Q_T, \\ U(t, 0) &= U_b(t), \quad U_x(t, 1) = 0 \quad \text{in } (0, T), \\ U(0, x) &= U_0(x) \quad \text{in } \Omega, \end{aligned} \quad (2.3)$$

with  $U_b = \ln(\alpha_b, \beta_b)$ ,  $U_0 = \ln(\alpha_0, \beta_0)$ ,  $Q(U) = q(e^U)$  and the new diffusion matrix is  $B(U) = A(e^U)\text{diag}(e^{U_1}, e^{U_2})$  and takes the form

$$B(r, s) = \begin{pmatrix} e^{2r} \left( \frac{3}{2} - e^r \right) & e^{r+s} \left( \frac{1}{2} - e^s \right) \\ e^{r+s} \left( \frac{1}{2} - e^r \right) & e^{2s} \left( \frac{3}{2} - e^s \right) \end{pmatrix}. \quad (2.4)$$

The matrix  $B(r, s)$  resulting of this transformation is still not positive definite. Nevertheless, in the case  $e^r + e^s \leq 1$  which is under interest,  $B(r, s)$  is positive definite. Moreover, this change of variables leads to nonnegative solutions, without using maximum principle, since  $\alpha = e^{U_1}$  and  $\beta = e^{U_2}$ .

### 3. Auxiliary problems

We will use a time discretization scheme to study (1.25)–(1.27). In order to prove global existence for the resulting stationary problem, it may be useful to introduce an artificial perturbation of the diffusion matrix  $A$  of type  $\varepsilon I$ , where  $\varepsilon > 0$  and  $I$  is the identity matrix (see the proof of Proposition 3.3 below and Lemma 3.6). Nevertheless, the choice of the parameter  $\varepsilon$  is technical and cannot be done independently of the time discretization parameter  $\tau$ . Here, we take  $\varepsilon = \tau$ , this choice being dictated by the sake of coherency of the discretization scheme proposed in Section 4. Indeed, in the case where  $\varepsilon$  is independent of  $\tau$ , this procedure is seriously compromised. More details on this question are given in Remark 3.8, at the end of this section. In summary, we need to solve the following problem:

$$\begin{aligned} \frac{1}{\tau}(u - \tilde{u}) - ((A(u) + \tau I)u_x)_x &= q(u) \quad \text{in } \Omega, \\ u(0) &= u_b, \quad u_x(1) = 0, \end{aligned} \quad (3.1)$$

where  $\tau > 0$  is a small parameter and  $\tilde{u} = \tilde{u}(x)$  is a fixed function. Before giving the existence result for this problem, let us define the solutions we deal with.

*Definition 3.1.*  $u = (\alpha, \beta) \in \mathbb{H}^1(\Omega)$  is said to be a weak solution of problem (3.1) if  $u(0) = u_b$ ,  $0 \leq \alpha, \beta$ ,  $\alpha + \beta \leq 1$  in  $\Omega$  and if for every  $\varphi \in \mathbb{H}_D^1(\Omega)$ , it holds

$$\frac{1}{\tau} \int_{\Omega} (u - \tilde{u}) \cdot \varphi \, dx + \int_{\Omega} (A(u) + \tau I) u_x \cdot \varphi_x \, dx = \int_{\Omega} q(u) \cdot \varphi \, dx. \quad (3.2)$$

We have the following result.

**Theorem 3.2.** *Let  $u_b = (\alpha_b, \beta_b) \in \mathbb{R}^2$  satisfy assumption (H2),  $\tilde{u} = (\tilde{\alpha}, \tilde{\beta}) \in \mathbb{L}^\infty(\Omega)$  such that  $0 < \tilde{\alpha}, \tilde{\beta}$ ,  $\tilde{\alpha} + \tilde{\beta} \leq 1$  a.e. in  $\Omega$  and  $\ln \tilde{u} \in \mathbb{L}^\infty(\Omega)$ . Then for all  $0 < \tau < 1$ , there exists a weak solution  $u_\tau = (\alpha_\tau, \beta_\tau) \in \mathbb{H}^1(\Omega)$  of the problem (3.1). Moreover,  $\ln u_\tau \in \mathbb{H}^1(\Omega)$  and it holds*

$$\int_{\Omega} (G_1(\alpha_\tau) + G_2(\beta_\tau)) \, dx + \frac{\tau}{4} \int_{\Omega} (|\alpha_{\tau x}|^2 + |\beta_{\tau x}|^2) \, dx \leq \int_{\Omega} (G_1(\tilde{\alpha}) + G_2(\tilde{\beta})) \, dx + C\tau, \quad (3.3)$$

where  $G_1$  and  $G_2$  are defined by (2.2).

For the proof, according to the change of unknown introduced in Section 2, we will consider the following stationary problem

$$\begin{aligned} \frac{1}{\tau} (e^U - e^{\tilde{U}}) - (B^\tau(U)U_x)_x &= Q^+(U) \quad \text{in } \Omega, \\ U(0) &= U_b, \quad U_x(1) = 0, \end{aligned} \quad (3.4)$$

where  $\tilde{U} = \ln \tilde{u}$ ,  $B^\tau$  is the matrix defined by

$$B^\tau = B^+ + D^\tau, \quad (3.5)$$

$B^+$  is given by

$$B^+(r, s) = \begin{pmatrix} e^{2r} \left( \frac{3}{2} - \min(e^r, 1 - e^s) \right) & e^{r+s} \left( \frac{1}{2} - e^s \right) \\ e^{r+s} \left( \frac{1}{2} - e^r \right) & e^{2s} \left( \frac{3}{2} - \min(e^s, 1 - e^r) \right) \end{pmatrix}, \quad (3.6)$$

and  $D^\tau$  is a diagonal matrix with

$$D_{11}^\tau(r, s) = D_{22}^\tau(s, r) = (e^{2r+s} + 5e^r(e^r + e^s))(e^r + e^s - 1)^+ + \tau e^r. \quad (3.7)$$

The vector field  $Q^+$  is defined by its components

$$\begin{aligned} Q_1^+(r, s) &= k_1 e^r (1 - e^r - e^s)^+ - \min(e^r, 1) (k_2 + k_3 \min(e^r + e^s, 1) + k_4 \min(e^s, 1)), \\ Q_2^+(r, s) &= \min(e^s, 1) (k_5 \min(e^s, (1 - e^r)^+) - k_6 (1 - e^r)^+ - k_7 \min(e^r, 1)). \end{aligned} \quad (3.8)$$

Clearly if  $e^r + e^s \leq 1$ , then  $B^+(r, s) = B(r, s)$ ,  $D_{11}^r(r, s) = D_{22}^r(s, r) = \tau e^r \rightarrow 0$  when  $\tau \rightarrow 0$  and  $Q^+(r, s) = Q(r, s)$ . In addition, we have for  $i = 1, 2$  that

$$|Q_i^+(r_1, r_2)| \leq C, \quad |Q_i^+(r_1, r_2)| \leq C e^{r_i}, \quad \forall (r_1, r_2) \in \mathbb{R}^2, \quad (3.9)$$

where  $C > 0$  depends only on  $k_i$ ,  $i = 1, \dots, 7$ . We will prove the following result.

**Proposition 3.3.** *Assume that  $\tilde{U} \in \mathbb{L}^\infty(\Omega)$  is such that  $\tilde{U}_1, \tilde{U}_2 \leq 0$  a.e. in  $\Omega$ . Then for all  $0 < \tau < 1$ , there exists a weak solution  $U_\tau \in H^1(\Omega)$  to problem (3.4).*

The proof of this result relies on the Leray-Schauder fixed point theorem, so we start by studying the linear problems associated with (3.4).

### 3.1. Linear problems associated with (3.4)

In the sequel, we let once for all  $0 < \tau < 1$  and  $\tilde{U} \in \mathbb{L}^\infty(\Omega)$  fixed. Let  $\bar{U} \in \mathbb{L}^\infty(\Omega)$  be given; we consider the following linear problem: find  $U \in \mathbb{H}^1(\Omega)$  satisfying

$$\begin{aligned} U(0) = U_b \quad \text{and} \quad \forall \varphi \in \mathbb{H}_D^1(\Omega), \\ \frac{1}{\tau} \int_{\Omega} (e^{\bar{U}} - e^{\tilde{U}}) \cdot \varphi \, dx + \int_{\Omega} B^r(\bar{U}) U_x \cdot \varphi_x \, dx = \int_{\Omega} Q^+(\bar{U}) \cdot \varphi \, dx. \end{aligned} \quad (3.10)$$

We have the following result.

**Lemma 3.4.** *For every  $\bar{U} \in \mathbb{L}^\infty(\Omega)$ , problem (3.10) has a unique solution  $U \in \mathbb{H}^1(\Omega)$ .*

*Proof.* We will apply the Lax-Milgram lemma. We set  $V = U - U_b$ , so (3.10) goes over into the following equivalent problem

$$\begin{aligned} V(0) = 0 \quad \text{and} \quad \forall \varphi \in \mathbb{H}_D^1(\Omega), \\ \int_{\Omega} B^r(\bar{U}) V_x \cdot \varphi_x \, dx = -\frac{1}{\tau} \int_{\Omega} (e^{\bar{U}} - e^{\tilde{U}}) \cdot \varphi \, dx + \int_{\Omega} Q^+(\bar{U}) \cdot \varphi \, dx. \end{aligned} \quad (3.11)$$

Next, we define a bilinear form  $\mathcal{A}$  on  $\mathbb{H}_D^1(\Omega) \times \mathbb{H}_D^1(\Omega)$  and a linear form  $\mathcal{L}$  on  $\mathbb{H}_D^1(\Omega)$  by setting

$$\mathcal{A}(V, \varphi) = \int_{\Omega} B^r(\bar{U}) V_x \cdot \varphi_x \, dx, \quad \mathcal{L}(\varphi) = -\frac{1}{\tau} \int_{\Omega} (e^{\bar{U}} - e^{\tilde{U}}) \cdot \varphi \, dx + \int_{\Omega} Q^+(\bar{U}) \cdot \varphi \, dx. \quad (3.12)$$

The continuity of  $\mathcal{A}$  and  $\mathcal{L}$  follows from the boundedness of  $\bar{U}$  and  $\tilde{U}$ . For the coerciveness of  $\mathcal{A}$ , it is sufficient to prove that the matrix  $D$  defined by

$$D(r, s) = B^+(r, s) + e^{r+s} (e^r + e^s - 1)^+ \text{diag}(e^r, e^s) \quad (3.13)$$



is positive definite. Let us compute  $D(r, s)\xi \cdot \xi$  for  $(r, s) \in \mathbb{R}^2$  and  $\xi = (\xi_1, \xi_2) \in \mathbb{R}^2$ . We consider first the case where  $e^r + e^s \leq 1$  so that

$$D(r, s)\xi \cdot \xi = e^{2r} \left( \frac{3}{2} - e^r \right) \xi_1^2 + e^{2s} \left( \frac{3}{2} - e^s \right) \xi_2^2 - e^{r+s} (e^r + e^s - 1) \xi_1 \xi_2. \quad (3.14)$$

The elementary inequality

$$1 - a - b \leq \sqrt{\frac{3}{2} - a} \sqrt{\frac{3}{2} - b} \quad \text{if } 0 \leq a, b, a + b \leq 1 \quad (3.15)$$

and Young inequality lead to

$$-e^{r+s} (e^r + e^s - 1) \xi_1 \xi_2 \geq -\frac{1}{2} \left( e^{2r} \left( \frac{3}{2} - e^r \right) \xi_1^2 + e^{2s} \left( \frac{3}{2} - e^s \right) \xi_2^2 \right), \quad (3.16)$$

so

$$D(r, s)\xi \cdot \xi \geq \frac{1}{2} \left( e^{2r} \left( \frac{3}{2} - e^r \right) \xi_1^2 + e^{2s} \left( \frac{3}{2} - e^s \right) \xi_2^2 \right) \geq \frac{1}{4} \min(e^{2r}, e^{2s}) \|\xi\|^2. \quad (3.17)$$

In the case  $e^r + e^s > 1$ , we have

$$D(r, s)\xi \cdot \xi = e^{2r} \left( \frac{1}{2} + e^s (e^r + e^s) \right) \xi_1^2 + e^{2s} \left( \frac{1}{2} + e^r (e^r + e^s) \right) \xi_2^2 - e^{r+s} (e^r + e^s - 1) \xi_1 \xi_2. \quad (3.18)$$

From the inequality

$$(1 - e^r - e^s)^2 \leq (e^r + e^s)^2 \leq \frac{9}{4} \left( \frac{1}{2} + e^s (e^r + e^s) \right) \left( \frac{1}{2} + e^r (e^r + e^s) \right), \quad (3.19)$$

we deduce that

$$e^r + e^s - 1 \leq \frac{3}{2} \sqrt{\frac{1}{2} + e^s (e^r + e^s)} \sqrt{\frac{1}{2} + e^r (e^r + e^s)}. \quad (3.20)$$

So, thanks to Young inequality we get

$$D(r, s)\xi \cdot \xi \geq \frac{1}{4} \left( e^{2r} \left( \frac{1}{2} + e^s (e^r + e^s) \right) \xi_1^2 + e^{2s} \left( \frac{1}{2} + e^r (e^r + e^s) \right) \xi_2^2 \right) \geq \frac{1}{8} \min(e^{2r}, e^{2s}) \|\xi\|^2. \quad (3.21)$$

Hence, we infer that for all  $\xi \in \mathbb{R}^2$ ,  $\bar{U} = (\bar{U}_1, \bar{U}_2) \in \mathbb{L}^\infty(\Omega)$ ,

$$B^\tau(\bar{U})\xi \cdot \xi \geq D(\bar{U})\xi \cdot \xi \geq \frac{1}{8} \min \left( e^{-2\|\bar{U}_1\|_{L^\infty(\Omega)}}, e^{-2\|\bar{U}_2\|_{L^\infty(\Omega)}} \right) \|\xi\|^2, \quad (3.22)$$

so Lax-Milgram lemma implies the existence of a unique solution  $V \in \mathbb{H}_D^1(\Omega)$  of problem (3.11). Consequently,  $U = V + U_b$  is the unique solution of (3.10).  $\square$

### 3.2. Proof of Proposition 3.3

Lemma 3.4 and the embedding  $H^1(\Omega) \subset L^\infty(\Omega)$  allow us to define the map  $\mathcal{S} : \mathbb{L}^\infty(\Omega) \rightarrow \mathbb{L}^\infty(\Omega)$ , by setting  $\mathcal{S}(\bar{U}) = U$  the solution of (3.10). We will establish, using the theorem of Leray Schauder, that  $\mathcal{S}$  has a fixed point  $U_\tau$  in  $\mathbb{L}^\infty(\Omega)$ , so  $U_\tau \in H^1(\Omega)$  is a solution of the nonlinear problem (3.4).

First, we prove that  $\mathcal{S}$  is continuous. Let  $(\bar{U}_n)_n$  be a sequence in  $\mathbb{L}^\infty(\Omega)$  such that  $\bar{U}_n \rightarrow \bar{U}$  strongly in  $\mathbb{L}^\infty(\Omega)$  as  $n \rightarrow \infty$  and let  $\mathcal{S}(\bar{U}_n) = U_n$ . We use the test function  $\varphi = U_n - U_b \in \mathbb{H}_D^1(\Omega)$  in (3.10), estimate (3.22), and Poincaré inequality to get

$$\frac{1}{\tau} \int_{\Omega} (e^{\tilde{U}} - e^{\bar{U}_n}) \cdot (U_n - U_b) dx + \int_{\Omega} Q^+(\bar{U}_n) \cdot (U_n - U_b) dx \geq C \|U_n - U_b\|_{\mathbb{H}^1(\Omega)}^2, \quad (3.23)$$

where  $C > 0$  is independent of  $n$ . So taking into account (3.9), we get, thanks to Young inequality,

$$\|U_n - U_b\|_{\mathbb{H}^1(\Omega)}^2 \leq C(\tau). \quad (3.24)$$

Thus,  $U_n$  is bounded in  $\mathbb{H}^1(\Omega)$  and from the compactness of the embedding  $H^1(\Omega) \hookrightarrow L^\infty(\Omega)$ , we deduce that there exists a subsequence of  $(U_n)_n$ , still denoted by  $(U_n)_n$  and a function  $U \in \mathbb{H}^1(\Omega)$  such that

$$U_n \longrightarrow U \quad \text{strongly in } \mathbb{L}^\infty(\Omega), \quad U_n \rightharpoonup U \quad \text{weakly in } \mathbb{H}^1(\Omega). \quad (3.25)$$

This implies the weak convergence  $B^\tau(\bar{U}_n)U_{nx} \rightharpoonup B^\tau(\bar{U})U_x$  in  $L^2(\Omega)$ , hence there exists a subsequence of  $(U_n)_n$  which converges towards  $\mathcal{S}(\bar{U})$ . Moreover thanks to the uniqueness result for the system (3.10), we see that all the sequence  $(U_n)_n$  converges to  $\mathcal{S}(\bar{U})$  which ends the proof of continuity of  $\mathcal{S}$ .

The compactness of  $\mathcal{S}$  follows from the compactness of the embedding  $H^1(\Omega)$  into  $L^\infty(\Omega)$  and (3.24). Finally, let us check that the sets  $\Lambda_\delta = \{\bar{U} \in \mathbb{L}^\infty(\Omega) / \bar{U} = \delta \mathcal{S}(\bar{U})\}$  are uniformly bounded with respect to  $\delta \in [0, 1]$ . Observe that  $\Lambda_0 = \{0\}$  and if  $\delta \neq 0$  the equation  $\bar{U} = \delta \mathcal{S}(\bar{U})$  is equivalent to  $\bar{U} \in \mathbb{H}^1(\Omega)$ ,  $\bar{U}(0) = \delta U_b$  and for all  $\varphi \in \mathbb{H}_D^1(\Omega)$ ,

$$\frac{1}{\tau} \int_{\Omega} (e^{\bar{U}} - e^{\tilde{U}}) \cdot \varphi dx + \frac{1}{\delta} \int_{\Omega} B^\tau(\bar{U})\bar{U}_x \cdot \varphi_x dx = \int_{\Omega} Q^+(\bar{U}) \cdot \varphi dx. \quad (3.26)$$

The remainder of the proof is a direct consequence of the following lemma.

**Lemma 3.5.** *Under the assumptions of Proposition 3.3, there exists a positive constant  $C(\tau)$  independent of  $\delta$  such that if  $\bar{U} \in \mathbb{H}^1(\Omega)$  satisfies (3.26), then it holds*

$$\|\bar{U}_x\|_{\mathbb{L}^2(\Omega)} \leq C(\tau). \quad (3.27)$$

For the proof, we need the following technical result which will be checked in the appendix.

**Lemma 3.6.** *For all  $(r, s), (\xi_1, \xi_2) \in \mathbb{R}^2$ , one has*

$$\begin{aligned} \mathcal{B}^r((r, s), (\xi_1, \xi_2)) &\equiv B_{11}^r(r, s)(1 + 2\tau e^{-r})\xi_1^2 + B_{22}^r(r, s)(1 + 2\tau e^{-s})\xi_2^2 \\ &+ (B_{12}^r(r, s)(1 + 2\tau e^{-r}) + B_{21}^r(r, s)(1 + 2\tau e^{-s}))\xi_1\xi_2 \geq \tau^2(\xi_1^2 + \xi_2^2), \end{aligned} \quad (3.28)$$

where  $B^r$  is the matrix given in (3.5).

*Proof of Lemma 3.5.* Testing the equation of (3.26) with  $\varphi = \bar{U} - \delta U_b + 2\tau(e^{-\delta U_b} - e^{-\bar{U}}) \in \mathbb{H}_D^1(\Omega)$  leads to

$$\int_{\Omega} \mathcal{B}^r(\bar{U}, \bar{U}_x) dx = -\frac{\delta}{\tau} \int_{\Omega} (e^{\bar{U}} - e^{\tilde{U}}) \cdot \varphi dx + \delta \int_{\Omega} Q^+(\bar{U}) \cdot \varphi dx. \quad (3.29)$$

The left-hand side is estimated using (3.28). We write  $\bar{U} = (\bar{U}_1, \bar{U}_2)$ ,  $\tilde{U} = (\tilde{U}_1, \tilde{U}_2)$ ,  $U_b = (U_{b1}, U_{b2})$ ; the convexity of  $e^s$  leads to

$$\begin{aligned} (e^{\bar{U}_i} - e^{\tilde{U}_i})(\bar{U}_i - \delta U_{bi}) &= (e^{\bar{U}_i}(\bar{U}_i - \delta U_{bi} - 1) + e^{\delta U_{bi}}) - (e^{\tilde{U}_i}(\tilde{U}_i - \delta U_{bi} - 1) + e^{\delta U_{bi}}) \\ &+ ((e^{\bar{U}_i} - e^{\tilde{U}_i}) - e^{\tilde{U}_i}(\bar{U}_i - \tilde{U}_i)) \geq f_i(\delta, \bar{U}_i) - f_i(\delta, \tilde{U}_i), \end{aligned} \quad (3.30)$$

where for  $i = 1, 2$ ,  $f_i(\delta, s) = e^s(s - \delta U_{bi} - 1) + e^{\delta U_{bi}} \geq 0$ , for all  $(\delta, s) \in [0, 1] \times \mathbb{R}$ . Using the elementary inequality  $e^s \geq 1 + s$ , valid for all  $s \in \mathbb{R}$ , we get

$$\begin{aligned} (e^{\bar{U}_i} - e^{\tilde{U}_i})(e^{-\delta U_{bi}} - e^{-\bar{U}_i}) &= (e^{\bar{U}_i - \delta U_{bi}} - \bar{U}_i + \delta U_{bi}) - (e^{\tilde{U}_i - \delta U_{bi}} - \tilde{U}_i + \delta U_{bi}) \\ &+ (e^{\tilde{U}_i - \bar{U}_i} - (\tilde{U}_i - \bar{U}_i) - 1) \geq g_i(\delta, \bar{U}_i) - g_i(\delta, \tilde{U}_i), \end{aligned} \quad (3.31)$$

with  $g_i(\delta, s) = e^{s - \delta U_{bi}} - s + \delta U_{bi} \geq 1$ , for all  $(\delta, s) \in [0, 1] \times \mathbb{R}$ . Combining (3.30) and (3.31), we find

$$\frac{-\delta}{\tau} \int_{\Omega} (e^{\bar{U}} - e^{\tilde{U}}) \cdot \varphi dx \leq \frac{1}{\tau} \int_{\Omega} (f_1(\delta, \tilde{U}_1) + f_2(\delta, \tilde{U}_2)) dx + 2 \int_{\Omega} (g_1(\delta, \tilde{U}_1) + g_2(\delta, \tilde{U}_2)) dx. \quad (3.32)$$

We recall that a.e. in  $\Omega$ ,  $-\|\tilde{U}_i\|_\infty \leq \tilde{U}_i \leq 0$  for  $i = 1, 2$ , and since the functions  $f_i, g_i$  are continuous on  $[0, 1] \times [-\|\tilde{U}_i\|_\infty, 0]$ , we deduce that the right-hand side of (3.32) is uniformly bounded with respect to  $\delta$ . Now we infer from (3.9) and Poincaré inequality that

$$\begin{aligned} \delta \int_{\Omega} Q^+(\bar{U}) \cdot (\bar{U} - U_b) dx &\leq C \int_{\Omega} |\bar{U} - U_b| dx \leq \frac{\tau^2}{2} \|\bar{U}_x\|_{L^2(\Omega)}^2 + C(\tau), \\ \delta \int_{\Omega} Q^+(\bar{U}) \cdot (e^{-\delta U_b} - e^{-\bar{U}}) dx &\leq C. \end{aligned} \quad (3.33)$$

The result follows by combining all these inequalities.  $\square$

### 3.3. End of proof of Theorem 3.2

Let  $U_\tau$  be the solution of (3.4) provided by Proposition 3.3. Recalling that  $\tilde{u} = e^{\tilde{U}}$  and  $u_b = e^{U_b}$ , we see that  $u_\tau = e^{U_\tau}$  satisfies the following problem:

$$\begin{aligned} \frac{1}{\tau} (u_\tau - \tilde{u}) - (A^\tau(u_\tau) u_{\tau x})_x &= Q^+(\ln u_\tau) \quad \text{in } \Omega, \\ u_\tau(0) = u_b, \quad u_{\tau x}(1) &= 0, \end{aligned} \quad (3.34)$$

where the matrix  $A^\tau$  is given by  $A^\tau(r, s) = A^+(r, s) + h^\tau(r, s)I$  with

$$\begin{aligned} A^+(r, s) &= \begin{pmatrix} r\left(\frac{3}{2} - \min(r, 1-s)\right) & r\left(\frac{1}{2} - s\right) \\ s\left(\frac{1}{2} - r\right) & s\left(\frac{3}{2} - \min(s, 1-r)\right) \end{pmatrix}, \\ h^\tau(r, s) &= (r+s-1)^+(rs+5(r+s)) + \tau. \end{aligned} \quad (3.35)$$

Note that if  $r+s \leq 1$  then  $A^+(r, s) = A(r, s)$  and  $h^\tau(r, s) = \tau$ .

We will focus on the  $L^\infty$  and  $\mathbb{H}^1$  estimates satisfied by the function  $u_\tau$ . We begin with the following  $L^\infty$  bounds.

**Lemma 3.7.** *Let the hypotheses of Theorem 3.2 hold, and let  $u_\tau = (\alpha_\tau, \beta_\tau) \in \mathbb{H}^1(\Omega)$  satisfy problem (3.34). One has*

$$0 < \alpha_\tau, \beta_\tau, \quad \alpha_\tau + \beta_\tau \leq 1 \quad \text{in } \Omega. \quad (3.36)$$

*Proof.* We write the equation satisfied by  $\alpha_\tau + \beta_\tau$  and test it with  $\varphi = (\alpha_\tau + \beta_\tau - 1)^+ \in H_D^1(\Omega)$ . We get using (1.24) that

$$\int_{\Omega} \frac{\alpha_\tau + \beta_\tau - (\tilde{\alpha} + \tilde{\beta})}{\tau} \varphi dx + \int_{\Omega} \left( \frac{1}{2} (\alpha_\tau + \beta_\tau) + h^\tau(\alpha_\tau, \beta_\tau) \right) |\varphi_x|^2 dx \leq 0, \quad (3.37)$$

so  $\int_{\Omega} (\alpha_{\tau} + \beta_{\tau} - (\tilde{\alpha} + \tilde{\beta})) \varphi dx \leq 0$ . Consequently,  $\int_{\Omega} \varphi^2 dx \leq \int_{\Omega} (\tilde{\alpha} + \tilde{\beta} - 1) \varphi dx \leq 0$ , and hence  $\alpha_{\tau} + \beta_{\tau} \leq 1$ .  $\square$

As a consequence of Lemma 3.7, we easily see that  $u_{\tau}$  is a solution to problem (3.1) in the sense of Definition 3.1. Moreover, since  $\ln u_{\tau} = U_{\tau} \in \mathbb{H}^1(\Omega)$  then  $\ln u_{\tau} \in \mathbb{L}^{\infty}(\Omega)$ . In order to check the entropy inequality (3.3), we test (3.1) with  $\varphi_{\tau} = \ln u_{\tau} - \ln u_b \in \mathbb{H}_D^1(\Omega)$  to get

$$\begin{aligned} \frac{1}{\tau} \int_{\Omega} (u_{\tau} - \tilde{u}) \cdot \varphi_{\tau} dx + \int_{\Omega} (1 - \alpha_{\tau} - \beta_{\tau}) \alpha_{\tau x} \beta_{\tau x} dx + \tau \int_{\Omega} \left( \frac{|\alpha_{\tau x}|^2}{\alpha_{\tau}} + \frac{|\beta_{\tau x}|^2}{\beta_{\tau}} \right) dx \\ + \int_{\Omega} \left( \left( \frac{3}{2} - \alpha_{\tau} \right) |\alpha_{\tau x}|^2 + \left( \frac{3}{2} - \beta_{\tau} \right) |\beta_{\tau x}|^2 \right) dx = \int_{\Omega} q(u_{\tau}) \cdot \varphi_{\tau} dx. \end{aligned} \quad (3.38)$$

Then, from (3.15) and Young inequality, we get

$$-\int_{\Omega} (\alpha_{\tau} + \beta_{\tau} - 1) \alpha_{\tau x} \beta_{\tau x} dx \geq -\frac{1}{2} \int_{\Omega} \left( \left( \frac{3}{2} - \alpha_{\tau} \right) |\alpha_{\tau x}|^2 + \left( \frac{3}{2} - \beta_{\tau} \right) |\beta_{\tau x}|^2 \right) dx, \quad (3.39)$$

so, inserting (3.39) into (3.38) and using the fact that  $3/2 - \alpha_{\tau}, 3/2 - \beta_{\tau} \geq 1/2$ , we see that

$$\frac{1}{\tau} \int_{\Omega} (u_{\tau} - \tilde{u}) \cdot \varphi_{\tau} dx + \frac{1}{4} \int_{\Omega} (|\alpha_{\tau x}|^2 + |\beta_{\tau x}|^2) dx \leq \int_{\Omega} q(u_{\tau}) \cdot \varphi_{\tau} dx. \quad (3.40)$$

Using the boundedness of  $q(u_{\tau})$  and the fact that the function  $s \ln(s)$  is bounded in  $[0, 1]$ , we obtain  $\int_{\Omega} q(u_{\tau}) \cdot \varphi_{\tau} dx \leq C$ , then the convexity of the functions  $G_1$  and  $G_2$  leads to

$$\int_{\Omega} (u_{\tau} - \tilde{u}) \cdot \varphi_{\tau} dx \geq \int_{\Omega} (G_1(\alpha_{\tau}) + G_2(\beta_{\tau})) dx - \int_{\Omega} (G_1(\tilde{\alpha}) + G_2(\tilde{\beta})) dx, \quad (3.41)$$

which ends the proof.

*Remark 3.8.* All the results of this section remain valid if one consider, instead of (3.1), the following problem:

$$\begin{aligned} \frac{1}{\tau} (u - \tilde{u}) - ((A(u) + \varepsilon I) u_x)_x &= q(u) \quad \text{in } \Omega, \\ u(0) &= u_b, \quad u_x(1) = 0, \end{aligned} \quad (3.42)$$

where  $\tau > 0$  and  $\varepsilon > 0$  is independent of  $\tau$ . In particular, the solution  $v_{\tau}^{\varepsilon}$  to (3.42) satisfies the  $L^{\infty}$  bounds and the entropy inequality given in Theorem 3.2, with the constant  $C > 0$  independent of  $\varepsilon$  (and  $\tau$ ). Thus performing the limit as  $\varepsilon \rightarrow 0$  in (3.42), we get a function  $v_{\tau}$  solving the problem

$$\begin{aligned} \frac{1}{\tau} (u - \tilde{u}) - (A(u) u_x)_x &= q(u) \quad \text{in } \Omega, \\ u(0) &= u_b, \quad u_x(1) = 0, \end{aligned} \quad (3.43)$$

which corresponds to the “natural” time discretization of our problem (1.25)–(1.27). However, from there, the situation becomes complicated because the obtained solution  $v_\tau$  to problem (3.43) has its components which are only nonnegative and we no longer have  $\ln v_\tau \in \mathbb{L}^\infty(\Omega)$  (in fact, we cannot even take the  $\ln$  of  $v_\tau$ ). Therefore, the time discretization scheme based on (3.43) cannot be solved.

## 4. Proof of Theorem 2.2

### 4.1. The time discretization scheme

Let assumptions (H1)–(H2) hold and let  $T > 0$ . We will use the backward Euler approximation of time derivative  $u_t \simeq (1/\tau)(u(t_k) - u(t_{k-1}))$ . We divide the time interval  $(0, T)$  into  $N$  subintervals  $(t_{k-1}, t_k]$  of the same length  $\tau = T/N$ . Then, we define recursively  $u_\tau^k$ ,  $k = 1, \dots, N$ , as the weak solution of (3.1) provided by Theorem 3.2 corresponding to the data  $\tilde{u} = u_\tau^{k-1}$ , that is,

$$\begin{aligned} \frac{1}{\tau} (u_\tau^k - u_\tau^{k-1}) - ((A(u_\tau^k) + \tau I)u_{\tau x}^k)_x &= q(u_\tau^k) \quad \text{in } \Omega, \\ u_\tau^k(0) &= u_b, \quad u_{\tau x}^k(1) = 0, \end{aligned} \quad (4.1)$$

$u_\tau^0$  being the initial condition  $u_0$  of problem (1.25)–(1.27). Let  $u^{(\tau)}, \bar{u}^{(\tau)}$  be the piecewise constant in time interpolation on  $(0, T)$  of  $u_\tau^1, u_\tau^2, \dots, u_\tau^N$  and  $u_\tau^0, u_\tau^1, \dots, u_\tau^{N-1}$ , respectively, that is,

$$u^{(\tau)}(t, x) = u_\tau^k(x), \quad \bar{u}^{(\tau)}(t, x) = u_\tau^{k-1}(x) \quad \text{on } (t_{k-1}, t_k] \times \Omega, \quad k = 1, \dots, N, \quad (4.2)$$

and let  $\tilde{u}^{(\tau)}$  be the function defined on  $Q_T$  by

$$\tilde{u}^{(\tau)}(t, x) = \frac{t - t_{k-1}}{\tau} (u^{(\tau)}(t, x) - \bar{u}^{(\tau)}(t, x)) + \bar{u}^{(\tau)}(t, x) \quad \text{on } (t_{k-1}, t_k] \times \Omega, \quad k = 1, \dots, N. \quad (4.3)$$

With these notations, we can rewrite (4.1) as

$$\begin{aligned} \tilde{u}_t^{(\tau)} - ((A(u^{(\tau)}) + \tau I)u_x^{(\tau)})_x &= q(u^{(\tau)}) \quad \text{in } \Omega, \\ u^{(\tau)}(0) &= u_b, \quad u_x^{(\tau)}(1) = 0. \end{aligned} \quad (4.4)$$

Now, we set for  $u_\tau^k = (\alpha_\tau^k, \beta_\tau^k)$

$$\begin{aligned} \eta_\tau^k &= \int_\Omega (G_1(\alpha_\tau^k) + G_2(\beta_\tau^k)) dx, \quad k = 0, \dots, N, \quad \eta_0 = \eta_\tau^0, \\ \eta^{(\tau)}(t) &= \eta_\tau^k, \quad \forall t \in (t_{k-1}, t_k], \quad k = 1, \dots, N. \end{aligned} \quad (4.5)$$

#### 4.2. Uniform estimates with respect to $\tau$

**Lemma 4.1.** Let  $u^{(\tau)} = (\alpha^{(\tau)}, \beta^{(\tau)})$  and  $\bar{u}^{(\tau)} = (\bar{\alpha}^{(\tau)}, \bar{\beta}^{(\tau)})$  defined by (4.2). One has

$$\begin{aligned} 0 < \alpha^{(\tau)}, \beta^{(\tau)}, \quad \alpha^{(\tau)} + \beta^{(\tau)} \leq 1 \quad \text{a.e. in } Q_T, \\ 0 < \bar{\alpha}^{(\tau)}, \bar{\beta}^{(\tau)}, \quad \bar{\alpha}^{(\tau)} + \bar{\beta}^{(\tau)} \leq 1 \quad \text{a.e. in } Q_T, \end{aligned} \quad (4.6)$$

and there exists a positive constant  $C$  independent of  $\tau$  such that

$$\|\eta^{(\tau)}\|_{L^\infty(0,T)}, \quad \|u^{(\tau)}\|_{L^2(0,T;\mathbb{H}^1(\Omega))}, \quad \|\bar{u}^{(\tau)}\|_{L^2(0,T;\mathbb{H}^1(\Omega))} \leq C. \quad (4.7)$$

*Proof.* We apply the results of Theorem 3.2, so the first part is immediate, then (3.3) leads to

$$\eta_\tau^k - \eta_\tau^{k-1} + \frac{\tau}{4} \int_{\Omega} (|\alpha_{\tau x}^k|^2 + |\beta_{\tau x}^k|^2) dx \leq C\tau, \quad k = 1, \dots, N. \quad (4.8)$$

Summing these inequalities from  $k = 1$  to  $k = m$ , for  $1 \leq m \leq N$ , we get

$$\eta_\tau^m - \eta_0 + \frac{\tau}{4} \sum_{k=1}^m \int_{\Omega} (|\alpha_{\tau x}^k|^2 + |\beta_{\tau x}^k|^2) dx \leq Cm\tau. \quad (4.9)$$

Therefore,

$$\max_{1 \leq m \leq N} \eta_\tau^m + \frac{1}{4} \sum_{k=1}^N \int_{\Omega} \tau (|\alpha_{\tau x}^k|^2 + |\beta_{\tau x}^k|^2) dx \leq \eta_0 + CT, \quad (4.10)$$

which can be written as

$$\|\eta^{(\tau)}\|_{L^\infty(0,T)} + \frac{1}{4} \int_{\Omega} \sum_{k=1}^N \int_{t_{k-1}}^{t_k} (|\alpha_{\tau x}^k|^2 + |\beta_{\tau x}^k|^2) dt dx \leq \eta_0 + CT. \quad (4.11)$$

This means that

$$\|\eta^{(\tau)}\|_{L^\infty(0,T)} + \frac{1}{4} \int_{Q_T} (|\alpha_x^{(\tau)}|^2 + |\beta_x^{(\tau)}|^2) dt dx \leq \eta_0 + CT. \quad (4.12)$$

Coming back to (4.9), we deduce that

$$\sum_{k=1}^{N-1} \int_{\Omega} \tau (|\alpha_{\tau x}^k|^2 + |\beta_{\tau x}^k|^2) dx = \int_{Q_T} |\bar{u}_x^{(\tau)}|^2 dt dx - \tau \int_{\Omega} |u_{0x}|^2 dx \leq 4(\eta_0 + CT), \quad (4.13)$$

and we get the result.  $\square$

We have also the following estimate.

**Lemma 4.2.** *There exists a positive constant  $C$  independent of  $\tau$  such that*

$$\|\tilde{u}^{(\tau)}\|_{H^1(0,T;(\mathbb{H}^1(\Omega))')} \quad \|\tilde{u}^{(\tau)}\|_{L^2(0,T;\mathbb{H}^1(\Omega))} \leq C, \quad (4.14)$$

$$\|\tilde{u}^{(\tau)} - u^{(\tau)}\|_{L^2(0,T;(\mathbb{H}^1(\Omega))')} \leq C\tau. \quad (4.15)$$

*Proof.* We use (4.4) and the results of Lemma 4.1 to deduce that  $\|\tilde{u}_t^{(\tau)}\|_{L^2(0,T;(\mathbb{H}^1(\Omega))')}$  is uniformly bounded. Now, since  $\tilde{u}_x^{(\tau)} = ((t - t_{k-1})/\tau)u_x^{(\tau)} + ((t_k - t)/\tau)\bar{u}_x^{(\tau)}$  on  $(t_{k-1}, t_k] \times \Omega$ , then thanks to Lemma 4.1 we deduce that  $\|\tilde{u}^{(\tau)}\|_{L^2(0,T;\mathbb{H}^1(\Omega))}$  is uniformly bounded. Finally, to check (4.15), we have from (4.3) that for  $t \in (t_{k-1}, t_k)$ ,  $\|\tilde{u}^{(\tau)} - u^{(\tau)}\|_{(\mathbb{H}^1(\Omega))'} = (t_k - t)\|\tilde{u}_t^{(\tau)}\|_{(\mathbb{H}^1(\Omega))'} \leq \tau\|\tilde{u}_t^{(\tau)}\|_{(\mathbb{H}^1(\Omega))'}$ . This leads to the result by using (4.14).  $\square$

### 4.3. Passing to the limit as $\tau \rightarrow 0$ : End of proof of Theorem 2.2

Using (4.14), we deduce the existence of a function  $u \in L^2(0, T; \mathbb{H}^1(\Omega)) \cap H^1(0, T; (\mathbb{H}^1(\Omega))')$  such that as  $\tau \rightarrow 0$  at least for some subsequence,

$$\tilde{u}^{(\tau)} \rightharpoonup u \quad \text{weakly in } L^2(0, T; \mathbb{H}^1(\Omega)) \cap H^1(0, T; (\mathbb{H}^1(\Omega))'). \quad (4.16)$$

Then Aubin compactness lemma and the compactness of the embedding of  $H^1(\Omega)$  into  $L^\infty$  lead to the strong convergence

$$\tilde{u}^{(\tau)} \longrightarrow u \quad \text{strongly in } L^2(0, T; \mathbb{L}^\infty(\Omega)). \quad (4.17)$$

Moreover, by Lemma 4.1, we infer the existence of a function  $v$  in  $L^2(0, T; \mathbb{H}^1(\Omega))$  and a subsequence of  $u^\tau$  such that

$$u^{(\tau)} \rightharpoonup v \quad \text{weakly in } L^2(0, T; \mathbb{H}^1(\Omega)), \quad (4.18)$$

and according to (4.15) and (4.16), we derive that  $v = u$ . Moreover, we have the strong convergence

$$u^{(\tau)} \longrightarrow u \quad \text{strongly in } \mathbb{L}^2(Q_T). \quad (4.19)$$

Indeed,

$$\begin{aligned} \|u^{(\tau)} - u\|_{L^2(Q_T)} &\leq \|u^{(\tau)} - \tilde{u}^{(\tau)}\|_{L^2(Q_T)} + \|\tilde{u}^{(\tau)} - u\|_{L^2(Q_T)} \\ &\leq C\|\tilde{u}^{(\tau)} - u^{(\tau)}\|_{L^2(0,T;\mathbb{H}^1(\Omega))}^{1/2} \|\tilde{u}^{(\tau)} - u^{(\tau)}\|_{L^2(0,T;(\mathbb{H}^1(\Omega))')}^{1/2} + \|\tilde{u}^{(\tau)} - u\|_{\mathbb{L}^2(Q_T)}. \end{aligned} \quad (4.20)$$



where  $C > 0$  is independent of  $\tau$ . Using (4.7), (4.14), (4.15), and (4.17), it is straightforward to deduce that  $u^{(\tau)} \rightarrow u$  strongly in  $\mathbb{L}^2(Q_T)$ , and hence a.e. in  $Q_T$ . Consequently,  $u = (\alpha, \beta)$  satisfies

$$0 \leq \alpha, \beta, \quad \alpha + \beta \leq 1, \quad \text{a.e. in } Q_T. \quad (4.21)$$

Finally, since  $H^1(0, T; (\mathbb{H}^1(\Omega))') \cap L^2(0, T; \mathbb{H}^1(\Omega)) \subset C^0([0, T]; \mathbb{L}^2(\Omega))$ , the initial condition is satisfied and thus  $u$  is a weak solution of (1.25)–(1.27) in the sense of Definition 2.1.

*Remark 4.3.* The result proved in this work remains valid if we replace the condition  $\lambda = \mu = P_0$  by one of these conditions:

$$\frac{8}{7} \max(\lambda, \mu) \leq P_0 \leq \frac{18}{7}(\lambda + \mu) \quad \text{or} \quad \frac{2}{3} \max(\lambda, \mu) \leq P_0 \leq \frac{8}{7} \min(\lambda, \mu). \quad (4.22)$$

Indeed, in these cases, direct calculations show that (3.15) becomes

$$(-2\mu b - 2\lambda a + 2P_0)^2 \leq \frac{9}{4}(2\lambda(1-a) + P_0)(2\mu(1-b) + P_0) \quad \text{if } 0 \leq a, b, a + b \leq 1. \quad (4.23)$$

## Appendix

### Proof of Lemma 3.6

Inequality (3.28) is equivalent to say that, for all  $(r, s) \in \mathbb{R}^2$ ,

$$\begin{aligned} & (B_{12}^r(r, s)(1 + 2\tau e^{-r}) + B_{21}^r(r, s)(1 + 2\tau e^{-s}))^2 \\ & \leq 4(B_{11}^r(r, s)(1 + 2\tau e^{-r}) - \tau^2)(B_{22}^r(r, s)(1 + 2\tau e^{-s}) - \tau^2). \end{aligned} \quad (A.1)$$

We write

$$((B_{12}^r(r, s)(1 + 2\tau e^{-r}) + B_{21}^r(r, s)(1 + 2\tau e^{-s}))^2 = \sum_{i=1}^6 I_i, \quad (A.2)$$

$I_i$  denoting the successive terms of the equality

$$\begin{aligned} \sum_{i=1}^6 I_i &= a^2 b^2 (a + b - 1)^2 + 4\tau^2 a^2 \left(a - \frac{1}{2}\right)^2 + 4\tau^2 b^2 \left(b - \frac{1}{2}\right)^2 \\ &+ 8\tau^2 ab \left(a - \frac{1}{2}\right) \left(b - \frac{1}{2}\right) + 4\tau a^2 b \left(a - \frac{1}{2}\right) (a + b - 1) + 4\tau ab^2 \left(b - \frac{1}{2}\right) (a + b - 1), \end{aligned} \quad (A.3)$$

with  $a = e^r$  and  $b = r^s$ . We split the proof into two cases.

Case 1. We suppose that  $a + b \leq 1$ , so that

$$\begin{aligned} B_{11}^r(r, s)(1 + 2\tau e^{-r}) - \tau^2 &= a^2 \left( \frac{3}{2} - a \right) + \tau a + 2\tau a \left( \frac{3}{2} - a \right) + \tau^2 = \sum_{i=1}^4 J_i, \\ B_{22}^r(r, s)(1 + 2\tau e^{-s}) - \tau^2 &= b^2 \left( \frac{3}{2} - b \right) + \tau b + 2\tau b \left( \frac{3}{2} - b \right) + \tau^2 = \sum_{i=1}^4 K_i, \end{aligned} \quad (\text{A.4})$$

where  $J_i$  and  $K_i$  denote, respectively, the successive terms of the first and second sums in (A.4). To handle  $I_1$ , we use (3.15) to see that

$$I_1 \leq a^2 b^2 \left( \frac{3}{2} - a \right) \left( \frac{3}{2} - b \right) = J_1 K_1. \quad (\text{A.5})$$

Next, to estimate the other terms, we use the inequality  $0 \leq 1 - a - b \leq 1$ , together with  $|c - 1/2| \leq 1/2 \leq (3/2 - c)$ , valid for  $c = a$  and  $c = b$ . We get successively that

$$\begin{aligned} I_2 \leq 2\tau^2 a^2 \left( \frac{3}{2} - a \right) &= 2J_1 K_4, & I_3 \leq 2\tau^2 b^2 \left( \frac{3}{2} - b \right) &= 2J_4 K_1, & I_4 \leq 4\tau^2 ab \left( \frac{3}{2} - b \right) &= 2J_2 K_3, \\ I_5 \leq 4\tau a^2 b \left( \frac{3}{2} - a \right) &= 4J_1 K_2, & I_6 \leq 4\tau ab^2 \left( \frac{3}{2} - b \right) &= 4J_2 K_1, \end{aligned} \quad (\text{A.6})$$

which concludes the proof in the first case.

Case 2. We suppose that  $a + b > 1$ , and we set  $B_{11}^r(r, s)(1 + 2\tau e^{-r}) - \tau^2 = f(a, b)$ , where

$$\begin{aligned} f(a, b) &= \sum_{i=1}^8 L_i = a^2 \left( \frac{1}{2} + b \right) + a^2 b(a + b - 1) + \tau a + 5a(a + b - 1)(a + b) \\ &\quad + 2\tau a \left( \frac{1}{2} + b \right) + 2\tau ab(a + b - 1) + 10\tau(a + b - 1)(a + b) + \tau^2. \end{aligned} \quad (\text{A.7})$$

Then,  $B_{22}^r(r, s)(1 + 2\tau e^{-s}) - \tau^2 = f(b, a)$ , and we set  $f(b, a) = \sum_{i=1}^8 M_i$ . Here again, the enumeration respects the ordering of the terms in each sum. First, we get from (3.19) that

$$I_1 \leq \frac{9}{4} a^2 b^2 \left( \frac{1}{2} + b + b(a + b - 1) \right) \left( \frac{1}{2} + a + a(a + b - 1) \right) = \frac{9}{4} (L_1 + L_2)(M_1 + M_2). \quad (\text{A.8})$$

Next, to estimate  $I_2$ , we distinguish two situations. If  $a \leq 1/2 + 1/\sqrt{2}$ , then  $(a - 1/2)^2 \leq 1/2 \leq 1/2 + b$  and

$$I_2 \leq 4\tau^2 a^2 \left( \frac{1}{2} + b \right) = 4L_1 M_8. \quad (\text{A.9})$$

Otherwise, we have  $a - 1/2 \leq 6(a + b - 1)$ , and

$$I_2 \leq 144\tau^2(a + b - 1)^2(a + b)^2 = \frac{36}{25}L_7M_7. \quad (\text{A.10})$$

Notice that  $I_3$  can be estimated in the same way. Now for  $I_4$ , since  $(a - 1/2)(b - 1/2) \leq (a + 1/2)(b + 1/2)$ , we see that

$$I_4 \leq 2L_5M_5. \quad (\text{A.11})$$

To estimate  $I_5$ , we consider first the case  $a \leq 3/2$ , so that we have

$$I_5 \leq 4\tau ab(a + b - 1)(a + b) = \frac{4}{5}L_3M_4, \quad (\text{A.12})$$

then if  $a > 3/2$ , the inequality  $a - 1/2 < 6(a + b - 1)$  leads to

$$I_5 \leq 24\tau b(a + b)^2(a + b - 1)^2 = \frac{12}{25}L_7M_4. \quad (\text{A.13})$$

$I_6$  can be estimated along the same lines as  $I_5$ , and we get the result.

## References

- [1] C. J. W. Breward, H. M. Byrne, and C. E. Lewis, "The role of cell-cell interactions in a two-phase model for avascular tumour growth," *Journal of Mathematical Biology*, vol. 45, no. 2, pp. 125–152, 2002.
- [2] C. J. W. Breward, H. M. Byrne, and C. E. Lewis, "A multiphase model describing vascular tumour growth," *Bulletin of Mathematical Biology*, vol. 65, no. 4, pp. 609–640, 2003.
- [3] H. M. Byrne, J. R. King, D. L. S. McElwain, and L. Preziosi, "A two-phase model of solid tumour growth," *Applied Mathematics Letters*, vol. 16, no. 4, pp. 567–573, 2003.
- [4] H. M. Byrne and L. Preziosi, "Modelling solid tumour growth using the theory of mixtures," *Mathematical Medicine and Biology*, vol. 20, no. 4, pp. 341–366, 2003.
- [5] T. L. Jackson and H. M. Byrne, "A mechanical model of tumor encapsulation and transcapsular spread," *Mathematical Biosciences*, vol. 180, no. 1, pp. 307–328, 2002.
- [6] L. Preziosi, *Cancer Modelling and Simulation*, Mathematical Biology and Medicine Series, Chapman & Hall/CRC, Boca Raton, Fla, USA, 2003.
- [7] D. Le, "Cross diffusion systems on  $n$  spatial dimensional domains," in *Proceedings of the 5th Mississippi State Conference on Differential Equations and Computational Simulations (Mississippi State, MS, 2001)*, vol. 10 of *Electronic Journal of Differential Equations*, pp. 193–210, Southwest Texas State University, San Marcos, Tex, USA, 2003.
- [8] P. Laurençot and D. Wrzosek, "A chemotaxis model with threshold density and degenerate diffusion," in *Nonlinear Elliptic and Parabolic Problems*, vol. 64 of *Progress in Nonlinear Differential Equations and Their Applications*, pp. 273–290, Birkhäuser, Basel, Switzerland, 2005.
- [9] L. Chen and A. Jüngel, "Analysis of a parabolic cross-diffusion population model without self-diffusion," *Journal of Differential Equations*, vol. 224, no. 1, pp. 39–59, 2006.
- [10] G. Galiano, A. Jüngel, and J. Velasco, "A parabolic cross-diffusion system for granular materials," *SIAM Journal on Mathematical Analysis*, vol. 35, no. 3, pp. 561–578, 2003.