Local existence and uniqueness of regular solutions in a model of tissue invasion by solid tumours

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Abstract

In this paper we consider a nonlinear system of differential equations arising in tumour invasion which has been proposed in [1]. The system consists of two PDEs describing the evolution of tumour cells and proteases and an ODE which models the concentration of the extracellular matrix. We prove local existence and uniqueness of solutions in the class of Hölder spaces. The proof of local existence is done by Schauder's fixed point theorem and for the uniqueness we use an idea from [2].

Keywords: Haptotaxis; Tumour invasion of tissue; Reaction-diffusion equations; Uniqueness.
AMS Subject Classification: 35K45, 35K57, 92C17

1 Introduction

The most dangerous feature of malignant tumour and the main cause of cancer deceases is the ability to metastasize. Metastasis is the formation of a secondary tumour foci at a site discontinuous from the primary tumour. Two main processes have to be taken into account during the metastasis.
The first one is called angiogenesis. Tumour cells response to hypoxia by secreting tumour angiogenic factors (TAFs) which induce to the endothelial cells in a nearby vessel to proliferate and migrate chemotactically towards the tumour.
The other important process occurring during metastasis is the invasion. Tumour cells on contact with extracellular matrix (ECM) induce the production of some proteolytic enzymes, such as metallo-proteases (MMPs) and serine-proteases. MMPs digest the ECM and this enables the cancer cells to migrate through the tissue.

In order to understand better the mechanisms leading to angiogenesis and invasion, several models were proposed. For the area related to angiogenesis we just refer to the recent review paper [3] and the references therein. Concerning tumour invasion modelling we briefly recapitulate some papers.

In [4] the authors proposed a model of invasion. In this model the diffusion of the tumour cells was neglected. They provided a travelling wave analysis for this model, finding a singular barrier which just can be crossed by the slowest member of the family of travelling waves connecting the steady-states. Later, in [5] the same system is studied but, by contrast with [4] where just regular travelling waves were founded, the authors showed travelling shock waves which jump over the singular barrier. In [6] basing on experimental data, the authors validate a model of invasion for the fibrosarcoma cell line HT1080. They showed that collagen concentration influences the proliferation of HT1080 in a biphasic manner. Recently, in [7] the author examined the role of the urokinase plasminogen system in cancer invasion, showing how this system influences the migratory properties of the cancer cells.

In this paper we will consider a model of tissue invasion that has been proposed by Chaplain and Anderson in the recent review book about cancer modelling [1]. They considered the following variables and facts.
Cancer Cells, n(x,t): The movement of cancer cells is supposed to be by a random motility and haptotaxis i.e. up to the spatial gradients in the extracellular matrix.
Extracellular Matrix, f(x,t): The matrix is just degraded by the proteases produced by the tumour.
Proteases, m(x,t): Factors influencing the protease concentration are assumed to be diffusion, production and natural decay.
As a result, the model reads as

$$\begin{aligned} \frac{\partial n}{\partial t} &= \overbrace{d_n \Delta n}^{\text{random motility}} \quad \overbrace{-\gamma \nabla \cdot (n \nabla f)}^{\text{haptotaxis}} && \text{in } \Omega \times (0,T), \\ \frac{\partial f}{\partial t} &= \overbrace{-\eta m f}^{\text{degradation}} && \text{in } \Omega \times (0,T), \\ \frac{\partial m}{\partial t} &= \overbrace{d_m \Delta m}^{\text{random motility}} \quad \overbrace{-\alpha m}^{\text{decay}} \quad \overbrace{+\beta n}^{\text{production}} && \text{in } \Omega \times (0,T), \end{aligned} \tag{1.1}$$

where $d_n, d_m, \alpha, \beta, \gamma$ and η are positive constants. Finally, denoting by ν the unit exterior vector to $\partial\Omega$, the model is supplemented with no-flux boundary conditions on $\partial\Omega$

$$\begin{cases} \dfrac{\partial n}{\partial \nu} - n\dfrac{\partial f}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0,T), \\ \dfrac{\partial m}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0,T), \end{cases} \tag{1.2}$$

and the initial conditions

$$\begin{cases} n(x,0) = n_0(x) & \text{in } \Omega, \\ f(x,0) = f_0(x) & \text{in } \Omega, \\ m(x,0) = m_0(x) & \text{in } \Omega. \end{cases} \tag{1.3}$$

In what follows and in order to simplify the formulas we will suppose $d_n = d_m = \eta = \alpha = \beta = \gamma = 1$. Let us point at that our calculations can be repeated without any problem for general positive constants.
This paper is organized as follows. In section 2 we define the space in which is our solution. In section 3 we prove the existence and uniqueness of local-in-time solution in such space.

2 Notations

In this paper $\Omega \subset \mathbb{R}^N$ is an open, connected set with regular boundary. $Q_T = \Omega \times (0,T)$ is a cylinder of $\mathbb{R}^{N+1}$. We consider the Banach space of Hölder continuous functions $H^{k+\alpha,(k+\alpha)/2}(\overline{Q}_T)$ where $k \geq 0$ is an integer and $\alpha \in (0,1)$. The associate norm to this space is given by

$$|u|^{k+\alpha}_{Q_T} := \langle u\rangle^{k+\alpha}_{x,Q_T} + \langle u\rangle^{(k+\alpha)/2}_{t,Q_T} + \sum_{j=0}^{k} \langle u\rangle^{j}_{Q_T},$$

where

$$\langle u\rangle^{j}_{Q_T} := \sum_{2r+s=k} \max_{Q_T} |D_t^r D_x^s u|_{Q_T},$$

$$\langle u\rangle^{k+\alpha}_{x,Q_T} := \sum_{2r+s=k} \langle D_t^r D_x^s u\rangle^{\alpha}_{x,Q_T},$$

$$\langle u\rangle^{k+\alpha}_{t,Q_T} := \sum_{0<\alpha+k-2r-s<2} \langle D_t^r D_s^s u\rangle^{(\alpha+k-2r-s)/2}_{t,Q_T},$$

and

$$\langle u\rangle^{\alpha}_{x,Q_T} := \sup_{\substack{(x,t),(x',t)\in\overline{Q}_T \\ |x-x'|\leq\rho_0}} \frac{|u(x,t)-u(x',t)|}{|x-x'|^{\alpha}}, \quad 0<\alpha<1,$$

$$\langle u\rangle_{t,Q_T} := \sup_{\substack{(x,t),(x,t')\in\overline{Q}_T \\ |t-t'|\leq\rho_0}} \frac{|u(x,t)-u(x,t')|}{|t-t'|^{\alpha}}, \quad 0<\alpha<1.$$

The norm in the space $L^p(\Omega)$, $1 \leq p \leq \infty$ is denoted by $\|\cdot\|_p$. The norm associated to the classical Sobolev spaces $W^{1,p}(\Omega)$ will be denoted by $\|\cdot\|_{1,p}$. Finally, the norm in the space $L^\infty(Q_T)$ is denoted by $\|\cdot\|_{\infty,Q_T}$.

3 Local existence and uniqueness of regular solutions

First of all we define a new variable $q = e^{-f}n$, then our system is transformed into

$$\begin{cases} \frac{\partial q}{\partial t} - \Delta q - \nabla q\cdot\nabla f = -qf_t = qmf & \text{in } \Omega\times(0,T), \\ \frac{\partial f}{\partial t} = -mf & \text{in } \Omega\times(0,T), \\ \frac{\partial m}{\partial t} = \Delta m - m + qe^f & \text{in } \Omega\times(0,T), \end{cases} \tag{3.1}$$

with a new boundary

$$\begin{cases} \frac{\partial q}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0,T), \\ \frac{\partial m}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0,T). \end{cases} \tag{3.2}$$

Actually, this change of variable has been proposed in another papers before as [8] and [9]. The main advantage of this change is that the first equation of the system is in divergence form.

In our proof, based on a fixed point argument, the following lemma will be required.

Lemma 3.1. *Let $N \le 3$. Given f such that $f \in H^{\alpha,\alpha/2}(\overline{Q}_T)$, $f_x \in H^{\alpha,\alpha/2}(\overline{Q}_T)$ then the problem*

$$\begin{cases} \frac{\partial q}{\partial t} - \Delta q - \nabla q \cdot \nabla f = qmf & \text{in } \Omega \times (0,T), \\ \frac{\partial m}{\partial t} = \Delta m - m + e^f q & \text{in } \Omega \times (0,T), \end{cases} \tag{3.3}$$

with Neumann boundary conditions and regular initial data admits a unique regular solution $(m,q) \in (H^{2+\alpha,1+\alpha/2}(Q_T))^2$. Moreover, if q_0, $m_0 \ge 0$ then $q(x,t), m(x,t) \ge 0$ for all $(x,t) \in Q_T$.

Proof. Consider the space of functions

$$X = \mathcal{C}([0,T]; L^2(\Omega)).$$

We define the operator $F : X \to X$ such that $F(\overline{q}) = m$ where m is the unique solution to the linear equation

$$\begin{cases} \frac{\partial m}{\partial t} = \Delta m - m + e^f \overline{q} & \text{in } \Omega \times 0,T), \\ \frac{\partial m}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0,T), \\ m(x,0) = m_0 & \text{in } \Omega. \end{cases} \tag{3.4}$$

On multiplying (3.4) by m and integrating in Q_T we obtain

$$\frac{\partial}{2\partial t}\int_0^T \|m\|_2^2 + \int_0^T \|\nabla m\|_2^2 + \int_0^T \|m\|_2^2 = \int_0^T \int_\Omega e^f \overline{q} m \tag{3.5}$$

Applying Hölder's inequality and Young's inequality to the right-hand-side of (3.5)

$$\frac{\partial}{2\partial t}\int_0^T \|m\|_2^2 + \int_0^T \|\nabla m\|_2^2 + \left(1 - \frac{1}{2\alpha}\|e^f\|_{\infty,Q_T}\right)\int_0^T \|m\|_2^2 \le \frac{\alpha}{2}\|e^f\|_{\infty,Q_T}\int_0^T \|\overline{q}\|_2^2. \tag{3.6}$$

Choosing $\alpha > 0$ large enough in (3.6) and integrating on the time interval $[0,T]$ we get

$$\|m(T)\|_2^2 \le \|m_0\|_2^2 + T\alpha\|e^f\|_{\infty,Q_T}\int_0^T \|\overline{q}\|_2^2. \tag{3.7}$$

Now, we define the linear operator $G : X \to X$ such that for each z $G(z)$ is the unique solution to

$$\begin{cases} \frac{\partial q}{\partial t} - \Delta q - \nabla q \cdot \nabla f = qzf & \text{in } \Omega \times 0, T), \\ \frac{\partial q}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0,T), \\ q(x,0) = q_0 & \text{in } \Omega. \end{cases} \tag{3.8}$$

It is easy to see that $q \in X$ is a fixed point of $H = G \circ F$ then is a weak solution to (3.3).

Taking $z = F(\overline{q}) = m$ and multiplying (3.8) by q we obtain, after integrating in space.

$$\frac{d}{2dt}\|q\|_2^2 + \|\nabla q\|_2^2 = \int_\Omega q^2 mf + \int_\Omega q \nabla q \cdot \nabla f. \tag{3.9}$$

From the Sobolev inequality $\|q\|_3 \le C\|q\|_{1,2}^{1/2}\|q\|_2^{1/2}$, $(N \le 3)$, Hölder's inequality and Young's inequality we infer

$$\frac{d}{2dt}\|q\|_2^2 + \|\nabla q\|_2^2 \le \|f\|_{\infty,Q_T}\|q\|_3\|q\|_6\|m\|_2 + \|\nabla f\|_{\infty,Q_T}\left(\frac{\alpha}{2}\|q\|_2^2 + \frac{1}{2\alpha}\|\nabla q\|_2^2\right) \le$$

$$\le C\|f\|_{\infty,Q_T}\|q\|_{1,2}^{3/2}\|q\|_2^{1/2}\|m\|_2 + \|\nabla f\|_{\infty,Q_T}\left(\frac{\alpha}{2}\|q\|_2^2 + \frac{1}{2\alpha}\|\nabla q\|_2^2\right) \le$$

$$\le \|f\|_{\infty,Q_T}(\alpha'\|q\|_{1,2}^2 + C_{\alpha'}\|q\|_2^2\|m\|_2^4) + \|\nabla f\|_{\infty,Q_T}\left(\frac{\alpha}{2}\|q\|_2^2 + \frac{1}{2\alpha}\|\nabla q\|_2^2\right).$$

Choosing $\alpha > 0$ large enough and $\alpha' > 0$ small enough then

$$\frac{d}{dt}\|q\|_2^2 \le (2\alpha'\|f\|_{\infty,Q_T} + 2C_{\alpha'}\|m\|_2^4 + \alpha\|\nabla f\|_{\infty,Q_T})\|q\|_2^2 := \beta(t)\|q\|_2^2.$$

If we choose $\overline{q}$ such that $\|\overline{q}\|_{\mathcal{C}([0,T];L^2(\Omega))} < \|q_0\|_2 + 1 = R$ then, thanks to the estimate (3.7) $\beta(t) \le M$ $\forall t \in (0,T)$, for that

$$\|q(t)\|_2^2 \le \|q_0\|_2^2 exp(tM), \ \ \forall t \in (0,T).$$

Clearly, choosing $\overline{T}$ small enough follows that $\|H(\overline{q}) = q\|_{\mathcal{C}([0,\overline{T}];L^2(\Omega))} \in B_R$. For that, $H : B_R \to B_R$. Now, we are going to prove that H is a contractive operator. Given $\overline{q}_1, \overline{q}_2 \in B_R$, then $F(\overline{q}_1) - F(\overline{q}_2) = m_1 - m_2$ satisfies the equation

$$\begin{cases} z_t - \Delta z + z = e^f(\overline{q}_1 - \overline{q}_2) & \text{in } \Omega \times (0,\overline{T}), \\ \frac{\partial z}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0,\overline{T}), \\ z(x,0) = 0 & \text{in } \Omega. \end{cases} \tag{3.10}$$

On multiplying (3.10) by $m_1 - m_2$ and integrating in Ω we obtain,

$$\frac{\partial}{\partial t}\|m_1 - m_2\|_2^2 \le C\|\overline{q}_1 - \overline{q}_2\|_2^2,$$

for that,

$$\|m_1 - m_2\|_{\mathcal{C}([0,\overline{T}];L^2(\Omega))} \leq C\sqrt{T}\|\overline{q}_1 - \overline{q}_2\|_{\mathcal{C}([0,\overline{T}];L^2(\Omega))}. \tag{3.11}$$

We have that $H(\overline{q}_1) - H(\overline{q}_2) = q_1 - q_2$ solves the equation

$$\begin{cases} z_t - \Delta z - \nabla z \cdot \nabla f = f m_1 z + f q_2 (m_1 - m_2) & \text{in } \Omega \times (0, \overline{T}), \\ \frac{\partial z}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0, \overline{T}), \\ z(x, 0) = 0 & \text{in } \Omega. \end{cases} \tag{3.12}$$

Multiplying (3.12) by $q_1 - q_2$ and integrating in Ω gives us

$$\frac{\partial}{2\partial t}\|q_1 - q_2\|_2^2 + \|\nabla(q_1 - q_2)\|_2^2 =$$

$$= \int_\Omega (q_1 - q_2)\nabla f \cdot \nabla(q_1 - q_2) + \int_\Omega f m_1 (q_1 - q_2)^2 + \int_\Omega f q_2 (m_1 - m_2)(q_1 - q_2) \leq$$

$$\leq \|\nabla f\|_{\infty, Q_{\overline{T}}}(\epsilon\|\nabla(q_1 - q_2)\|_2^2 + C_\epsilon\|q_1 - q_2\|_2^2) +$$

$$+ \|f\|_{\infty, Q_{\overline{T}}}(\alpha'\|\nabla(q_1 - q_2)\|_2^2 + (\alpha' + C_{\alpha'}\|m_1\|_2^4)\|q_1 - q_2\|_2^2) +$$

$$\|f\|_{\infty, Q_{\overline{T}}}(\epsilon'(\|q_1 - q_2\|_2^2 + \|\nabla(q_1 - q_2)\|_2^2) + C_{\epsilon'}\|q_2\|_3^2\|m_1 - m_2\|_2^2).$$

Choosing $\alpha', \epsilon, \epsilon'$ positive and small enough we infer

$$\frac{\partial}{\partial t}\|q_1 - q_2\|_2^2 \leq \alpha(t)\|m_1 - m_2\|_2^2 + \beta\|q_1 - q_2\|_2^2,$$

where β is a positive constant and $\alpha(t) = C_{\epsilon'}\|f\|_{\infty, Q_{\overline{T}}}\|q_2\|_3^2$. Then,

$$\frac{\partial}{\partial t}\left(e^{-\beta t}\|q_1 - q_2\|_2^2\right) \leq \alpha(t) e^{-\beta t}\|m_1 - m_2\|_2^2. \tag{3.13}$$

From the Sobolev's inequality $\|q_2\|_3^2 \leq C\|q_2\|_{1,2}^{1/2}\|q_2\|_2^{1/2}$ and taking in account that $q_2 \in \mathcal{C}([0,\overline{T}]; L^2(\Omega)) \cap L^2(0, \overline{T}; H^1(\Omega))$ we get

$$\int_0^{\overline{T}} \alpha(s) ds \leq M. \tag{3.14}$$

Finally thanks to (3.14) and (3.11) we obtain

$$\|H(\overline{q}_1) - H(\overline{q}_2)\|_{\mathcal{C}([0,\overline{T}];L^2(\Omega))} \leq C\sqrt{Me^{\beta\overline{T}}}\sqrt{\overline{T}}\|\overline{q}_1 - \overline{q}_2\|_{\mathcal{C}([0,\overline{T}];L^2(\Omega))}.$$

Choosing $T \leq \overline{T}$ small enough, $H : B_R \to B_R$ is contractive and from Banach's fixed point theorem we infer that problem (3.3) have a unique solution in the space

$$\mathcal{C}([0, T]; L^2(\Omega)) \cap L^2(0, T; H^1(\Omega)).$$

Since $N \leq 3$ then the function $q \in L^2(0,T;L^6(\Omega))$. We begin an iterative argument that will provided us regularization of our solution. Let $p = 6$, multiplying by pm^{p-1} the second equation of (3.3) and integrating by parts, gives us

$$\frac{\partial}{\partial t}\|m\|_p^p + \frac{4(p-1)}{p}\|\nabla(m^{p/2})\|_2^2 + p\|m\|_p^p = p\int_\Omega e^f q m^{p-1} \leq$$

$$\leq p\|e^f\|_{\infty,Q_T}\|q\|_p\|m^{p/2}\|_2\|m\|_p^{\frac{p-2}{2}} \leq p\|e^f\|_{\infty,Q_T}(C_\alpha\|q\|_p^2\|m\|_p^{p-2} + \alpha\|m^{p/2}\|_2^2).$$

Choosing $\alpha > 0$ small enough the following estimate follows

$$\frac{\partial}{\partial t}\|m\|_p^p \leq pM\|q\|_p^2\|m\|_p^{p-2}.$$

From this differential inequality we infer

$$\|m(t)\|_p^2 \leq \|m_0\|_p^2 + \int_0^t \frac{p^2}{2}M\|q(s)\|_p^2 ds, \tag{3.15}$$

for all $t \in [0,T]$. Since $q \in L^2(0,T;L^p(\Omega))$ then the integral term on the right-hand-side of (3.15) is finite. Therefore $m \in L^\infty(0,T;L^6(\Omega))$.

On multiplying the first equation (3.3) by pq^{p-1}, then after integrating by parts, we obtain

$$\frac{\partial}{\partial t}\|q\|_p^p + \frac{4(p-1)}{p}\|\nabla(q^{p/2})\|_2^2 = p\int_\Omega q^{p-1}\nabla u\cdot\nabla f + p\int_\Omega q^p m f. \tag{3.16}$$

Now, we are going to find the proper bounds of the two integrals on the right-hand-side.

$$\begin{aligned} p\int_\Omega q^{p-1}\nabla q\cdot\nabla f &\leq \|\nabla f\|_{\infty,Q_T}(C_\epsilon\|q^{p/2}\|_2^2 + \epsilon p^2\|q^{\frac{p}{2}-1}\nabla q\|_2^2) \\ &= \|\nabla f\|_{\infty,Q_T}(C_\epsilon\|q\|_p^p + 4\epsilon\|\nabla(q^{p/2})\|_2^2). \end{aligned} \tag{3.17}$$

Taking in account that $m \in L^\infty(0,T;L^6(\Omega))$ we get for $p = 6$ that

$$\begin{aligned} p\int_\Omega q^p m f &\leq p\|f\|_{\infty,Q_T}\|q^{p/2}\|_2\|q^{p/2}\|_3\|m\|_6 \\ &\leq p\|f\|_{\infty,Q_T}\|q^{p/2}\|_2^{3/2}\|q^{p/2}\|_{1,2}^{1/2}\|m\|_6 \\ &\leq p\|f\|_{\infty,Q_T}\|q^{p/2}\|_2\|q^{p/2}\|_{1,2}\|m\|_6 \\ &\leq \|f\|_{\infty,Q_T}(\epsilon'\|q^{p/2}\|_{1,2}^2 + p^2C_{\epsilon'}\|q^{p/2}\|_2^2\|m\|_6^2) \\ &\leq \|f\|_{\infty,Q_T}(\epsilon'\|q^{p/2}\|_{1,2}^2 + p^2MC_{\epsilon'}\|q^{p/2}\|_2^2). \end{aligned} \tag{3.18}$$

Choosing ϵ, ϵ' small enough and putting the estimates (3.17), (3.18) in (3.16) we obtain

$$\frac{\partial}{\partial t}\|q\|_p^p + \|\nabla(q^{p/2})\|_2^2 \leq Cp^2\|q\|_p^p.$$

Easily after integrating on $[s,t] \subset [0,T]$, implies

$$\|q(t)\|_p^p + \int_s^t \|\nabla(q^{p/2})\|_2^2 \leq exp(Cp^2(t-s))\|q(s)\|_p^p. \tag{3.19}$$

From (3.19) and following the same argument as in [10, p. 1197] we can prove that $q \in L^\infty(Q_T)$. However, for completeness we present it here.
Consider any $\bar{t} \in (0, T]$. For simplicity $\bar{t} = T$, although this argument remains true for every $\bar{t} \in (0, T]$. Take $t_0 \in (T-1, T)$, $\sigma = 3$. Define $p_m = 6\sigma^m$ and $\delta_m = (T - t_0)\sigma^{-2m-1}$. Observe that $p_m^2 \delta_m = c$. Now, consider the intervals $I_m = [T - \sigma\delta_m, T - \delta_m]$. We define the sequence $N_m = \sup_{\tau\in[t_m,T]} \|q(\tau)\|_{p_m}$ where $t_m \in I_m$ will be determined later. If we apply (3.19) with $s = t_{m+1}$ and $\tau \in [t_{m+1}, T]$ then

$$N_{m+1} = \sup_{\tau\in[t_{m+1},T]} \|q(\tau)\|_{p_{m+1}} \leq (exp(Cp_{m+1}^2 \sigma\delta_{m+1}))^{1/p_{m+1}} \|q(t_{m+1})\|_{p_{m+1}} \tag{3.20}$$

We have to determine $\|q(t_{m+1})\|_{p_{m+1}}$. Thanks to the Sobolev's embedding,

$$\|q(t_{m+1})\|_{p_{m+1}}^{p_m} = \|q^{p_m/2}(t_{m+1})\|_6^2 \leq M(\|q(t_{m+1})\|_{p_m}^{p_m} + \|\nabla(q^{p_m/2}(t_{m+1}))\|_2^2) \tag{3.21}$$

We are going to determine $\|\nabla(q^{p_m/2}(t_{m+1}))\|_2^2$. Applying (3.19) for $s = t_m$ and $t = T - \delta_{m+1}$ (so $I_{m+1} \subset [s, t]$) we get

$$\inf_{\tau\in I_{m+1}} \|\nabla(q^{p_m/2}(\tau))\|_2^2 \leq |I_{m+1}|^{-1} exp(Cp_m^2(T - \delta_{m+1} - t_m))\|q(t_m)\|_{p_m}^{p_m}.$$

Choosing $t_{m+1} = \tau$ we obtain the estimate we were looking for. Since $|I_{m+1}| < 1$ then with a similar argument we can estimate $\|q(t_{m+1})\|_{p_m}^{p_m}$. Putting this estimate in (3.21) we get

$$\begin{aligned} \|q(t_{m+1})\|_{p_{m+1}}^{p_m} &\leq 2\sigma^2(\sigma^3 - 1)^{-1}\delta_m^{-1} exp(Cp_m^2(1 - \sigma^{-2})\delta_m)\|q(t_m)\|_{p_m}^{p_m} \\ &\leq C\delta_m^{-1} N_m^{p_m} \end{aligned} \tag{3.22}$$

Thanks to (3.22) and taking in account that $p_m^2 \delta_m = C_1$, we obtain from (3.20)

$$\begin{aligned} N_{m+1} &\leq (exp(M)^{1/\sigma} C\delta_m^{-1})^{1/p_m} N_m \\ &\leq \left(\prod_{i=0}^{m} (C_2\sigma^{2i})^{1/p_i}\right) N_0 = z_m N_0 \end{aligned}$$

Clearly z_m is finite for all m because $\ln z_m = \sum_{i=0}^m \frac{1}{6\sigma^i}(\ln C_2 + 2i \ln \sigma)$ where $\sigma > 1$. Finally,

$$\|q(T)\|_\infty \leq \sup_{m\geq 1} N_m \leq C_3 N_0 \leq C_3 \sup_{\tau\in[0,T]} \|q(\tau)\|_6 < \infty.$$

Repeating the same argument for m we get the same regularity. Now, the regularity can be improved thanks to [11, Chapter 3, Theorem 10.1] and [11, Chapter 3, Theorem 12.1] , the first one gives us $q, m \in H^{\alpha,\alpha/2}(Q_T)$ and then we can apply the second one obtaining $q, m \in H^{2+\alpha,1+\alpha/2}(Q_T)$. Since fm is bounded in $L^\infty(Q_T)$ then, from maximum principle for parabolic equations we get the positivity of q. Now, from the positivity of q we can infer, thanks to the maximum principle, the positivity of m.

Theorem 3.2. *If the initial condition (1.3) are regular then the problem given by (1.1) with the boundary condition (1.2) and initial condition (1.3) respectively, has a unique local solution in the space* $(H^{2+\alpha,1+\alpha/2}(Q_T))^3$.

Proof. We define the following ball in $H = \{f : f \in H^{\alpha,\alpha/2}(Q_T) \wedge f_x \in H^{\alpha,\alpha/2}(Q_T)\}$

$$B_\delta(f_0) = \{u : |u - f_0|^\alpha_{Q_T} < \delta \wedge |(u - f_0)_x|^\alpha_{Q_T} < \delta\}.$$

Now, we define the operator $K : B_\delta(f_0) \to H$. $K(\overline{f})$ is the unique solution to the ordinary differential equation

$$\frac{\partial f}{\partial t} = -mf, \;\; f(x, 0) = f_0(x),$$

where m is given as the solution to the second equation in (3.3) with $f = \overline{f}$. For simplify the calculus, we consider $f_0 = 1$, the same calculus can be done with a general f_0. We have,

$$f(x,t) = 1 + \int_0^t -m(x,s)f(x,s)ds = 1 + \int_0^t -m(x,s)e^{-\int_0^s m(x,\theta)d\theta}$$

By definition $|f - 1|^\alpha_{Q_T} = \langle f - 1\rangle^\alpha_{x,Q_T} + \langle f - 1\rangle^{\alpha/2}_{t,Q_T} + \max_{Q_T} |f - 1|$.

$$\langle f - 1\rangle^\alpha_{x,Q_T} := \sup_{\substack{(x,t),(x',t)\in\overline{Q}_T\\ |x-x'|\le\rho_0}} \frac{|\int_0^t -m(x,s)e^{-\int_0^s m(x,\theta)d\theta} + \int_0^t -m(x',s)e^{-\int_0^s m(x',\theta)d\theta}|}{|x - x'|^\alpha} \le$$

$$\le \sup_{\substack{(x,t),(x',t)\in\overline{Q}_T\\ |x-x'|\le\rho_0}} \frac{\|m\|_{\infty,Q_T}\left(\int_0^t ds \int_0^s |m(x',\theta) - m(x,\theta)|d\theta\right) + \int_0^t |m(x,s) - m(x',s)|ds}{|x - x'|^\alpha} \le$$

$$\le T^2\|m\|_{\infty,Q_T}\langle m\rangle^\alpha_{x,Q_T} + T\langle m\rangle^\alpha_{x,Q_T}$$

$$\langle f - 1\rangle^{\alpha/2}_{t,Q_T} := \sup_{\substack{(x,t),(x,t')\in\overline{Q}_T\\ |t-t'|\le\rho_0}} \frac{|\int_0^t -m(x,s)e^{-\int_0^s m(x,\theta)d\theta} + \int_0^{t'} -m(x,s)e^{-\int_0^s m(x,\theta)d\theta}|}{|t - t'|^{\alpha/2}} \le$$

$$\le \sup_{\substack{(x,t),(x',t)\in\overline{Q}_T\\ |t-t'|\le\rho_0}} \frac{|\int_t^{t'} m(x,s)e^{-\int_0^s m(x,\theta)d\theta}|}{|t - t'|^{\alpha/2}} \le |t - t'|^{1-\alpha/2}\|m\|_{\infty,Q_T}$$

$$\max_{Q_T} |f - 1| \le T\|m\|_{\infty,Q_T}$$

Also by definition $|(f - 1)_x|^\alpha_{Q_T} = \langle f_x\rangle^\alpha_{x,Q_T} + \langle f_x\rangle^{\alpha/2}_{t,Q_T} + \max_{Q_T} |f_x|$

$$(f - 1)_x = \int_0^t e^{-\int_0^s m(x,\theta)d\theta}\left(-m_x(x,s) + m(x,s)\int_0^s m_x(x,\theta)d\theta\right)$$

Let denote $a_x = e^{-\int_0^s m(x,\theta)d\theta}$, $b_x = m(x,s)$, $c_x = \int_0^s m_x(x,\theta)d\theta$ and $d_x = m_x(x,s)$ then

$$\langle (f - 1)_x\rangle^\alpha_{x,Q_T} := \sup_{\substack{(x,t),(x',t)\in\overline{Q}_T\\ |x-x'|\le\rho_0}} \frac{|\int_0^t a_x(-d_x + b_xc_x) - a_{x'}(-d_{x'} + b_{x'}c_{x'})ds|}{|x - x'|^\alpha} \le$$

$$\leq \sup_{\substack{(x,t),(x',t)\in\overline{Q}_T\\|x-x'|\leq\rho_0}} \frac{|\int_0^t a_x(d_{x'}-d_x)+d_{x'}(a_{x'}-a_x)+a_xb_xc_x-a_{x'}b_{x'}c_{x'}|}{|x-x'|^\alpha}\leq$$

$$\leq T\max_{Q_T}\langle m_x\rangle^\alpha_{x,Q_T}+\|m_x\|_{\infty,Q_T}T^2\langle m\rangle^\alpha_{x,Q_T}+$$

$$+\sup_{\substack{(x,t),(x',t)\in\overline{Q}_T\\|x-x'|\leq\rho_0}} \frac{|\int_0^t(a_x-a_{x'})b_xc_x+a_{x'}(b_x-b_{x'})c_x+a_{x'}b_{x'}(c_x-c_{x'})|}{|x-x'|^\alpha}\leq$$

$$\leq T\langle m_x\rangle^\alpha_{x,Q_T}+\|m_x\|_{\infty,Q_T}T^2\langle m\rangle^\alpha_{x,Q_T}+T^3\langle m\rangle^\alpha_{x,Q_T}\|m\|_{\infty,Q_T}\|m_x\|_{\infty,Q_T}+$$
$$+T^2\|m_x\|_{\infty,Q_T}\langle m\rangle^\alpha_{x,Q_T}+T^2\|m\|_{\infty,Q_T}\langle m_x\rangle^\alpha_{x,Q_T}$$

After some calculations, we obtain

$$\langle (f-1)_x\rangle^{\alpha/2}_{t,Q_T}\leq |t-t'|^{1-\alpha/2}(\|m_x\|_{\infty,Q_T}+T\|m\|_{\infty,Q_T}\|m_x\|_{\infty,Q_T}).$$

$$\max_{Q_T}|f-1|\leq T(\|m_x\|_{\infty,Q_T}+\|m\|_{\infty,Q_T}\|m_x\|_{\infty,Q_T}).$$

Given $\overline{f}\in\overline{B}_\delta(f_0)$ from Lemma 3.1 we infer the existence of a unique $m\in H^{2+\alpha,1+\alpha/2}(Q_T)$. Moreover, thanks to the estimates we have of $K(\overline{f})$ in H, we can clearly choose T small enough such that $K(\overline{f})\in B_\delta(f_0)$. The operator K is compact, indeed $K(\overline{f})\in H^{2+\alpha,1+\alpha/2}(Q_T)$ which is compactly embedded in H. Therefore Schauder's fixed point theorem gives us the existence of f, solution of our system. Then from f we can obtain recursively m and q. For the uniqueness we will use an idea from [2]. Let (n_1,f_1,m_1), (n_2,f_2,m_2) two solutions of the system and consider the function

$$g(n_1,n_2)=n_1\ln n_1+n_2\ln n_2-(n_1+n_2)\ln\left(\frac{n_1+n_2}{2}\right)$$

Since $g(n_1(0),n_2(0))=g(n_0,n_0)=0$ then, after integrating in $\Omega\times(0,t)$, and following [2, p. 89] we have

$$\int_\Omega g(n_1(t),n_2(t))=$$
$$=-\int_0^t\int_\Omega\frac{n_1n_2}{n_1+n_2}\left|\nabla\ln\left(\frac{n_1}{n_2}\right)\right|^2+\int_0^t\int_\Omega\frac{n_1n_2}{n_1+n_2}\nabla\ln\left(\frac{n_1}{n_2}\right)\cdot(\nabla f_1-\nabla f_2)$$
$$\leq-\frac{1}{2}\int_0^t\int_\Omega\frac{n_1n_2}{n_1+n_2}\left|\nabla\ln\left(\frac{n_1}{n_2}\right)\right|^2+\frac{1}{8}\|n_1+n_2\|_{\infty,Q_T}\int_0^t\int_\Omega|\nabla(f_1-f_2)|^2$$

Now, we are going to find a bound for the second integral on the right-hand-side. We will suppose, only for simplify the notation, that $f_0\equiv 1$. We know that $f_1=e^{-\int_0^t m_1}$ and $f_2=e^{-\int_0^t m_2}$. We have that

$$\int_0^t\|\nabla f_1-\nabla f_2\|_2^2=$$
$$=\int_0^t\int_\Omega\left\{e^{-\int_0^s m_2}\left(\int_0^s\nabla(m_2-m_1)\right)-\left(\int_0^s\nabla m_1\right)\left(e^{-\int_0^s m_1}-e^{-\int_0^s m_2}\right)\right\}^2\leq$$

As $(a+b)^2 \leq 2(a^2+b^2)$ and $\nabla m_1 \in L^\infty(Q_T)$ then

$$\leq C\left\{\int_0^t \int_\Omega \left(\int_0^s \nabla(m_2-m_1)\right)^2 - \left(\int_0^s (m_2-m_1)\right)^2\right\}$$

Applying Jensen's Inequality and Fubini's Theorem we obtain

$$\leq C\left\{\int_0^t s\left(\int_0^s \|\nabla(m_2-m_1)\|_2^2 + \int_0^s \|m_1-m_2\|_2^2\right)\right\}.$$

Consider the functions $\varphi(s) = \int_0^s \|\nabla(m_2-m_1)\|_2^2$ and $\psi(s) = \int_0^s \|m_2-m_1\|_2^2$. Since, are nondecreasing functions, then

$$\int_0^t (\varphi(s)+\psi(s))ds \leq \int_0^t (\varphi(t)+\psi(t))ds = t(\varphi(t)+\psi(t))$$

For that,

$$\int_0^t \|\nabla f_1 - \nabla f_2\|_2^2 \leq C\left(\int_0^t \|\nabla(m_2-m_1)\|_2^2 + \int_0^t \|m_2-m_1\|_2^2\right)$$

Multiplying the equation that satisfies $m_1 - m_2$ by $(m_1-m_2)_t$ easily can be proved

$$\|\nabla(m_2-m_1)(t)\|_2^2 + \|(m_2-m_1)(t)\|_2^2 \leq C\|n_1+n_2\|_{\infty,Q_T}\int_0^t \|\sqrt{n}_1 - \sqrt{n}_2\|_2^2$$

Putting all the estimates together we have

$$\int_\Omega g(n_1(t),n_2(t)) + \|\nabla(m_2-m_1)(t)\|_2^2 + \|(m_2-m_1)(t)\|_2^2 \leq$$

$$\leq C\|n_1+n_2\|_{\infty,Q_T}\left\{\int_0^t \|\sqrt{n}_1-\sqrt{n}_2\|_2^2 + \int_0^t \|\nabla(m_2-m_1)\|_2^2 + \int_0^t \|m_2-m_1\|_2^2\right\}.$$

Finally the uniqueness follows combining [2, Lemma 4.6]

$$g(n_1,n_2) \geq (\sqrt{n}_1 - \sqrt{n}_2)^2$$

and Gronwall's Lemma.

Acknowledgments

C. Morales-Rodrigo gratefully acknowledges support from the EU Marie Curie Research Training Network Grant *"Modelling, Mathematical Methods and Computer Simulations of Tumour Growth and Therapy"*, contract number MCRTN-CT-2004-503661.

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