Theoretical and numerical analysis for a hybrid tumor model with diffusion depending on vasculature

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Abstract

In this work we analyse a PDE-ODE problem modelling the evolution of a Glioblastoma, which includes an anisotropic nonlinear diffusion term with a diffusion velocity increasing with respect to vasculature. First, we prove the existence of global in time weak-strong solutions using a regularization technique via an artificial diffusion in the ODE-system and a fixed point argument. In addition, stability results of the critical points are given under some constraints on parameters. Finally, we design a fully discrete finite element scheme for the model which preserves the pointwise and energy estimates of the continuous problem.

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1 Introduction

In this paper we investigate the following parabolic PDE-ODE system

\[
\begin{align*}
\frac{\partial T}{\partial t} - \nabla \cdot ((\kappa_1 P(\Phi, T) + \kappa_0) \nabla T) &= f_1(T, N, \Phi) \quad \text{in} \quad (0, T_f) \times \Omega \\
\frac{\partial N}{\partial t} &= f_2(T, N, \Phi) \quad \text{in} \quad (0, T_f) \times \Omega \\
\frac{\partial \Phi}{\partial t} &= f_3(T, N, \Phi) \quad \text{in} \quad (0, T_f) \times \Omega
\end{align*}
\]

endowed with non-flux boundary condition

\[
\frac{\partial T}{\partial n} \bigg|_{\partial \Omega} = 0 \quad \text{on} \quad (0, T_f) \times \partial \Omega
\]

where \(n\) is the outward unit normal vector to \(\partial \Omega\) and initial conditions

\[
T(0, \cdot) = T_0, \quad N(0, \cdot) = N_0, \quad \Phi(0, \cdot) = \Phi_0 \quad \text{in} \quad \Omega.
\]
Here $\Omega \subset \mathbb{R}^3$ is a smooth bounded domain, $T_f > 0$ the final time, and $T(t,x), N(t,x)$ and $\Phi(t,x)$ represent the tumor and necrotic densities and the vasculature concentration at the point $x \in \Omega$ and time $t > 0$, respectively. We have chosen $\Omega \subset \mathbb{R}^3$ although the dimension of the domain will not have influence on our study as we see along the paper. The nonlinear reaction terms are:

\[
\begin{align*}
  f_1(T,N,\Phi) &:= \rho T P(\Phi,T) \left( 1 - \frac{T + N + \Phi}{K} \right) - \alpha T \sqrt{1 - P(\Phi,T)^2} - \beta_1 N T, \\
  f_2(T,N,\Phi) &:= \alpha T \sqrt{1 - P(\Phi,T)^2} + \beta_1 N T + \delta T \Phi + \beta_2 N \Phi, \\
  f_3(T,N,\Phi) &:= \gamma T \sqrt{1 - P(\Phi,T)^2} \frac{\Phi}{K} \left( 1 - \frac{T + N + \Phi}{K} \right) - \delta T \Phi - \beta_2 N \Phi,
\end{align*}
\]

where $\kappa_1, \kappa_0 > 0$ are diffusion coefficients, $\rho, \alpha, \beta_1, \beta_2, \delta, \gamma > 0$ are reaction coefficients and $K > 0$ is the maximum population size that can be sustained by the environment (see Table 1 and [14, 17, 18] for a description of the parameters):

| Variable | Description | Value |
|----------|-------------|-------|
| $\kappa_1$ | Anisotropic speed diffusion | $cm^2$/day |
| $\kappa_0$ | Isotropic diffusion | $cm^2$/day |
| $\rho$ | Tumor proliferation rate | day$^{-1}$ |
| $\alpha$ | Hypoxic death rate | cell/day |
| $\beta_1$ | Change rate from tumor to necrosis | day$^{-1}$ |
| $\beta_2$ | Change rate from vasculature to necrosis | day$^{-1}$ |
| $\gamma$ | Vasculature proliferation rate | day$^{-1}$ |
| $\delta$ | Vasculature destruction by tumor | day$^{-1}$ |
| $K$ | Carrying capacity | cell/cm$^3$ |

Table 1: Coefficients.

The vasculature volume fraction function $P(\Phi,T)$ is defined as follows

\[
P(\Phi,T) = \Phi_+ \left( \frac{\Phi_+ + K}{2} \right) + T_+
\]

with $T_+ = \max\{0,T\}$ and similar to $\Phi_+$. Notice that $P(\Phi,T)$ is continuous in $\mathbb{R}^2$, satisfies the pointwise estimates

\[
0 \leq P(\Phi,T) \leq 1 \quad \forall (T,\Phi) \in [0,K] \times [0,K]
\]

and $P(\Phi,T) = 0$ for $\Phi = 0$ (without vasculature) and $P(\Phi,T) = 1$ for $(\Phi,T) = (K,0)$ (maximum of vasculature).

It is well-known that Glioblastoma (GBM) presents pathologically important differences with respect to other brain tumors of lesser malignancy. Given the great difficulties presented by the treatment of GBM, the mathematical modelling of GBM has been a relatively broad topic in the applied mathematics community. However, the applicability of the results has been very reduced [3, 17, 19, 23].

Our system (1.1)–(1.3) models some biological aspects of the evolution of the Glioblastoma (GBM). In [11], we analysed a simplified model of (1.1)–(1.3) with linear diffusion ($\kappa_1 = 0$) where we did a study of classical solution. Moreover, we explained the relation between biological effects and reaction terms.

Following the recommendation of Molab group, which classifies the GBM depending on the width

[http://matematicas.uclm.es/molab/](http://matematicas.uclm.es/molab/)
of the tumor ring and/or the tumor surface regularity (see [23, 24] respectively) using image treatment about GBM or more recently, working with a PDE-ODE system with linear diffusion in [22], we study (1.1)-(1.3) where we have included a nonlinear diffusion term in the spatial mobility of the tumor with the diffusion velocity increasing with vasculature. In fact, the diffusion term in (1.1)-(1.3) includes the nonlinear term, $\kappa_1 P(\Phi, T)$, and the linear self-diffusion term with coefficient $\kappa_0 > 0$, what makes the diffusion non-degenerate (although from a biological point of view $\kappa_0$ must be small). Therefore, tumor cells show a random movement when there is not nutrient limitation (included in the linear self-diffusion term) whereas they have a kinematic movement when there exists a nutrient limitation. Thus, we express this possible lack of nutrient through function $P(\Phi, T)$ which measures the quotient between the amount of vasculature and the amount of vasculature and tumor together.

The inclusion of this nonlinear diffusion term makes our model more realistic than model studied in [11], but it entails technical complications that we try to overcome in this work. Specifically, the main contributions of the paper are the following:

1. The existence of global in time weak solutions of (1.1)-(1.3). For that, we regularize (1.1)-(1.3) including an artificial diffusion in the ODE-system. This regularized problem maintains the same pointwise estimates as (1.1)-(1.3) and it is solved by a fixed point argument. Finally, we get some estimates for the solution of regularized problem which let us to pass to the limit arriving at one solution of (1.1)-(1.3).

2. We investigate the asymptotic behaviour of (1.1)-(1.3). Mainly, we prove that the vasculature tends to zero "pointwisely" as time goes to infinity and, under some constraints on the parameters, tumor also goes to the extinction and necrosis grows to a upper limit. Looking at the asymptotic behaviour of the linear diffusion problem (see [11, Section 4]), we conclude that the nonlinear diffusion model has a similar behaviour.

3. The construction of an uncoupled and linear numerical scheme of (1.1)-(1.3) by means of a implicit-explicit finite difference scheme in time and a finite element with "mass-lumping" approximation in space which preserves the pointwise and energy estimates of the continuous model whenever an acute triangulation is considered.

There exist many studies dedicated to the analysis of PDE-ODE systems in the literature, see for instance [4, 6, 7, 11, 15, 16, 21, 25] and the references therein. Some of them such as [15, 25], use results of classical solutions given in [1, 2]. On the other hand, in [16], the study of a PDE-ODE system is based on approximating regularized problems pointwise estimates. Moreover, the results obtained in [16] are used in a recent work of the same authors for other PDE-ODE system, see [28]. In a previous paper [11], we have studied the PDE-ODE system (1.1)-(1.3) with linear diffusion ($\kappa_1 = 0$) where we get existence and uniqueness of classical solution using a fixed point argument. Now, due to the complexity of the nonlinear diffusion term, we will prove existence of a so-called weak-strong solution (see Definition 3.1 below). Roughly speaking, it will be a variational solution for the tumor-PDE and pointwise for the ODE system with necrosis and vasculature variables.

There are multiple results according to the analysis of the Finite Element (FE) scheme which preserves pointwisely and energy estimates related to parabolic PDEs with maximum principle, see for instance [8]. Specifically, in order to obtain pointwisely estimates for FE numerical scheme of nonlinear PDE-ODE systems with maximum principle, we highlight works such as [10] [26] [27] or [5] where it is considered an acute triangulation to have the pointwisely estimates and [13] for energy estimates. Another relevant paper in the study of FE method for nonlinear PDE is [20] where the authors use a mass-lumping technique with quadrature formula.

The outline of the paper is as follows. In Section 2, we present preliminary results which we will use along the study of system (1.1)-(1.3). In Section 3 we prove the existence of weak-strong solutions of (1.1)-(1.3). Section 4 is dedicated to the long time behaviour of the solution. Finally, in Section
we present a numerical scheme of our model (1.1)-(1.3) which preserves the same estimates as the continuous model.

2 Preliminaries

In this section we include some necessary results to study the existence of solutions of the system (1.1)-(1.3).

The regularity of the functions \( P(\Phi, T) \) and \( f_i(T, N, \Phi) \) for \( i = 1, 2, 3 \) (see [11] Lemma 2) can be summarized in the following lemma

**Lemma 2.1.** The functions \( P : \mathbb{R}^2 \to \mathbb{R} \) and \( f_i : \mathbb{R}^3 \to \mathbb{R} \) for \( i = 1, 2, 3 \) defined in (1.5) and (1.4), are continuous and locally lipschitz.

In order to define the concepts of weak and strong solution for a parabolic problem, we introduce the following "weak" space

\[
W_2 = \left\{ u \in L^\infty(0, T_f; H^1(\Omega)) \cap L^2(0, T_f; H^2(\Omega)) : \quad u_t \in L^2(0, T_f; (H^1(\Omega))^\prime) \right\} ,
\]

and the "strong" space

\[
S_2 = \left\{ u \in L^\infty(0, T_f; H^1(\Omega)) \cap L^2(0, T_f; H^2(\Omega)) , \quad u_t \in L^2(0, T_f; L^2(\Omega)) \right\} .
\]

\( W_2 \) and \( S_2 \) are Banach spaces with the respective norms:

\[
\| u \|_{W_2} = \| u \|_{L^\infty(0, T_f; L^2(\Omega))} + \| u \|_{L^2(0, T_f; H^2(\Omega))} + \| u_t \|_{L^2(0, T_f; (H^1(\Omega))^\prime)},
\]

\[
\| u \|_{S_2} = \| u \|_{L^\infty(0, T_f; H^1(\Omega))} + \| u \|_{L^2(0, T_f; H^2(\Omega))} + \| u_t \|_{L^2(0, T_f; L^2(\Omega))}.
\]

Along the paper the constant \( C \) will denote different constants which will appear in the work.

In these circumstances, we will use the following result about existence and uniqueness of weak and strong solution for a linear parabolic problem, see for instance [3].

**Theorem 2.1.** Given \( \Omega \subseteq \mathbb{R}^3 \) a bounded open set and \((0, T_f)\) a time interval for a fixed time \( T_f > 0 \), we consider the following linear parabolic problem

\[
\begin{aligned}
\begin{cases}
\quad u_t + Lu = f & \text{in} \quad (0, T_f) \times \Omega, \\
\quad u(0, \cdot) = u_0 & \text{in} \quad \Omega, \\
\quad \frac{\partial u}{\partial n} |_{\partial \Omega} = 0 & \text{on} \quad (0, T_f) \times \partial \Omega
\end{cases}
\end{aligned}
\]

where \( f \in L^2(0, T_f; L^2(\Omega)) \),

\[
Lu = -\sum_{i,j=1}^3 \left( a_{ij}(t, x) \ u_{x_j} \right)_{x_i} + \sum_{i=1}^3 b_i(t, x) u_{x_i} + c(t, x) u
\]

denotes a second-order partial elliptic differential operator with \( a_{ij}, b_i, c \in L^\infty(0, T_f; L^\infty(\Omega)) \), \( a_{ij} = a_{ji} \) and there exists \( C > 0 \) such that

\[
\sum_{i,j=1}^3 a_{ij}(t, x) p_i p_j \geq C \| p \|^2, \quad \text{a.e.} \quad (t, x) \in (0, T_f) \times \Omega, \quad \forall p \in \mathbb{R}^3.
\]

Then:
a) For every $u_0 \in L^2(\Omega)$, (2.3) has a unique weak solution $u \in \mathcal{W}_2$ and
\[
\|u\|_{\mathcal{W}_2} \leq C \left( \|u_0\|_{L^2(\Omega)} , \|f\|_{L^2(0,T_f;L^2(\Omega))} \right).
\]
b) Assume $a_{ij} = \delta_{ij}$ (Kronecker delta) for $i, j = 1, 2, 3$ hence
\[
Lu = -\Delta u + \sum_{i=1}^{3} b_i(t,x) u_x + c(t,x) u.
\]

Then, for every $u_0 \in H^1(\Omega)$, (2.3) has a unique strong solution $u \in \mathcal{S}_2$ and
\[
\|u\|_{\mathcal{S}_2} \leq C \left( \|u_0\|_{H^1(\Omega)} , \|f\|_{L^2(0,T_f;L^2(\Omega))} \right).
\]

Finally, we will use the following fixed point theorem to obtain solution of (1.1)-(1.3)

**Theorem 2.2 (Leray-Schauder’s theorem).** Let $V$ a Banach space, $\lambda \in [0,1]$ and $\mathcal{R} : V \to V$ a continuous and compact map such that for every $v \in V$ with $v = \lambda \mathcal{R}(v)$, satisfies that $\|v\|_V \leq C$ with $C > 0$ independent of $\lambda \in [0,1]$. Then, there exists a fixed point $v$ of $\mathcal{R}$.

## 3 Existence of Solution of Problem (1.1)-(1.3)

We assume along the paper the following assumptions on the initial data
\[
0 \leq T_0(x), N_0(x), \Phi_0(x) \leq K, \quad \text{a.e. } x \in \Omega. \tag{3.1}
\]

First of all, we define the concept of solution used in the paper.

**Definition 3.1 (Weak-Strong solution of (1.1)-(1.3)).** Given $T_0 \in L^\infty(\Omega)$ and $N_0, \Phi_0 \in H^1(\Omega) \cap L^\infty(\Omega)$ satisfying (3.1), then $(T, N, \Phi)$ is called a weak-strong solution of problem (1.1)-(1.3) if $T \in \mathcal{W}_2$, $N, \Phi \in L^\infty(0,T_f;H^1(\Omega))$, $N_t, \Phi_t \in L^2(0,T_f;L^2(\Omega))$ and they satisfy
\[
\int_0^{T_f} (T_t, v)_{(H^1(\Omega))'} \, dt + \int_0^{T_f} \int_\Omega (\kappa_1 P(\Phi, T) + \kappa_0) \nabla T \cdot \nabla v \, dx \, dt = \int_0^{T_f} \int_\Omega f_1(T,N,\Phi) \, v \, dx \, dt,
\]

\[
\forall v \in L^2(0,T_f;H^1(\Omega)) \quad \text{and}
\]

\[
\begin{cases}
N_t = f_2(T,N,\Phi) & \text{a.e. in } (0,T_f) \times \Omega \\
\Phi_t = f_3(T,N,\Phi)
\end{cases}
\]

and the boundary and initial conditions (1.2) and (1.3) are satisfied by $T$ and $(T,N,\Phi)$, respectively.

### 3.1 Truncated problem

In order to obtain a solution of (1.1)-(1.3), we define the following truncated system of (1.1):

\[
\begin{align*}
\frac{\partial T}{\partial t} - \nabla \cdot \left( (\kappa_1 P(\Phi^K_+,T^K_+) + \kappa_0) \nabla T \right) &= f_1 \left( T^K_+,N^{C(T_f)}_+,\Phi^K_+ \right) \\
\frac{\partial N}{\partial t} &= f_2 \left( T^K_+,N^{C(T_f)}_+,\Phi^K_+ \right) \\
\frac{\partial \Phi}{\partial t} &= f_3 \left( T^K_+,N^{C(T_f)}_+,\Phi^K_+ \right)
\end{align*}
\]

subject to (1.2) and (1.3). We have denoted $T^K_f = \min \{ K, \max \{0,T\} \}$ and similar to $\Phi^K_+$ and $N^{C(T_f)}_+$.
with $C \(T_f\)$ an exponential positive constant which depends on the final time $T_f > 0$ and the carrying capacity $K$ (see [11] Lemma 5)).

Once we obtain the existence of solution of the truncated problem (3.2), we will prove that this solution is also a positive solution of (1.1)-(1.3), due to the following estimates for any possible weak-strong solution of (3.2).

**Lemma 3.1.** Any weak-strong solution $(T, N, \Phi)$ of (3.2) with initial data satisfying (3.1) satisfies the following bounds:

a) **Pointwise estimates:**

\[ 0 \leq T, \Phi \leq K \quad \text{and} \quad 0 \leq N \leq C \(T_f\), \quad \text{a.e. in} \quad \(0, T_f\) \times \Omega. \]  

(3.3)

b) **Energy estimates:**

\[ \|T\|_{L^\infty(0,T_f;L^2(\Omega))} + \|T\|_{L^2(0,T_f;H^1(\Omega))} \leq C \left( \|T_0\|_{L^2(\Omega)}, K, |\Omega|, T_f \right). \]

**Proof.** a) Let $(T, N, \Phi)$ a weak-strong solution of (3.2). Since one can rewrite $f_1(T, N, \Phi) = T \tilde{f}_1(T, N, \Phi)$, multiplying the first equation of (3.2) by $T_- = \min \{T, 0\}$ and integrating in $\Omega$, we get

\[ \frac{1}{2} \frac{d}{dt} \int_\Omega (T_-)^2 \, dx + \int_\Omega (\kappa_1 P (\Phi^K_+, T^K_+) + \kappa_0) \, \nabla T_- \, dx = 0, \quad \text{a.e. in} \quad (0, T_f). \]

Hence, since $T_-(0, x) = 0$, then $T_-(t, x) = 0$ a.e. $(t, x) \in (0, T_f) \times \Omega$. To obtain the upper bound $T \leq K$, we multiply the first equation of (3.2) by $(T - K)_+ = \max \{0, T - K\}$ and integrate in $\Omega$

\[ \frac{1}{2} \frac{d}{dt} \int_\Omega ((T - K)_+)^2 \, dx + \int_\Omega (\kappa_1 P (\Phi^K_+, T^K_+) + \kappa_0) \, \nabla (T - K)_+ \, dx = 0, \quad \text{a.e. in} \quad (0, T_f). \]

Since $f_1(T^K_+, N^{C(T)}_+, \Phi^K_+) \leq \rho \, T^K_+ \left( 1 - \frac{T^K_+}{K} \right)$, then

\[ f_1 \left( T^K_+, N^{C(T)}_+, \Phi^K_+ \right) (T - K)_+ \leq \rho \, T^K_+ \left( 1 - \frac{T^K_+}{K} \right) (T - K)_+ = 0. \]

Since $(T(0, x) - K)_+ = 0$, then $(T(t, x) - K)_+ = 0$ a.e. $(t, x) \in (0, T_f) \times \Omega$.

For the corresponding bounds of $N$ and $\Phi$ given in (3.3), we can use the same argument as in [11] Lemma 5].

b) Using the pointwise bounds for $(T, N, \Phi)$ given in a), multiplying the first equation of (3.2) by $T$ and integrating in $\Omega$, we get

\[ \frac{1}{2} \frac{d}{dt} \int_\Omega T^2 \, dx + \int_\Omega (\kappa_1 P (\Phi^K_+, T^K_+) + \kappa_0) \, \nabla T \, dx = \int_\Omega T^2 \tilde{f}_1(T, N, \Phi) \leq \int_\Omega \rho T^2 \, dx \leq \rho \, K^2 \, |\Omega|. \]

Integrating in time, the proof is finished. \[\square\]
By Lemma \(3.1\) a), for any \((T, N, \Phi)\) a weak-strong solution of (3.2), we deduce that \(T^K_+ = T, \ N^C(T_+^+) = N\) and \(\Phi^K_+ = \Phi\) and then, \(f_i(T^K_+, N^C(T_+^+), \Phi^K_+) = f_i(T, N, \Phi)\) for \(i = 1, 2, 3\). Hence, we obtain the following crucial corollary

**Corollary 3.1.** If \((T, N, \Phi)\) is a weak-strong solution of the truncated problem (3.2), then \((T, N, \Phi)\) is also a weak-strong solution of (1.1)-(1.3) and \((T, N, \Phi)\) satisfies the pointwise bounds (3.3).

### 3.2 Existence of Weak-Strong Solution of Problem (3.2)

**Theorem 3.1.** There exists a weak-strong solution \((T, N, \Phi)\) of (3.2) in the sense of Definition 3.1

**Remark 3.1.** We can not guarantee the uniqueness of the weak-strong solution of (1.1), (1.3) due to \(T\) is not sufficiently regular by the influence of the nonlinear diffusion. Notice that, unlike in [11] and due to nonlinear diffusion, we are not able to prove that \(T\) is a pointwise solution of (1.1). Consequently, the uniqueness of weak-strong solution is an open problem.

**Proof.** The proof of this theorem follows the next steps:

1. Regularize the problem via an artificial diffusion with parameter \(\epsilon > 0\) for \((N, \Phi)\).
2. Solve the regularized problem for any fixed value of \(\epsilon\).
3. Taking limits \(\epsilon \rightarrow 0\) to get solution of the non-regularized problem (3.2).

**Step 1. Regularizing the problem (3.2)**

We will study the following family of regularized problems related to system (3.2). For any \(\epsilon > 0\). We define \((T_\epsilon, N_\epsilon, \Phi_\epsilon)\) as the solution of

\[
\begin{align*}
\frac{\partial T}{\partial t} \ - \ \nabla \cdot \left( (\kappa_1 \ P (\Phi^K_+, T^K_+) + \kappa_0) \ \nabla \ T \right) &= f_1(T^K_+, N^C(T_+^+), \Phi^K_+) \\
\frac{\partial N}{\partial t} - \epsilon \ \Delta \ N &= f_2(T^K_+, N^C(T_+^+), \Phi^K_+) \\
\frac{\partial \Phi}{\partial t} - \epsilon \ \Delta \ \Phi &= f_3(T^K_+, N^C(T_+^+), \Phi^K_+)
\end{align*}
\]

(3.4)

with the boundary conditions

\[
\frac{\partial T}{\partial n} \bigg|_{\partial \Omega} = \epsilon \ \frac{\partial N}{\partial n} \bigg|_{\partial \Omega} = \epsilon \ \frac{\partial \Phi}{\partial n} \bigg|_{\partial \Omega} = 0
\]

(3.5)

and the initial conditions

\[
T \big|_{t=0} = T_0, \ N \big|_{t=0} = N_0, \ \Phi \big|_{t=0} = \Phi_0 \ \text{in} \ \Omega.
\]  

(3.6)

Now, we can define the kind of solution which we will obtain

**Definition 3.2 (Weak-Strong solution of (3.4)-(3.6)).** Given \(T_0 \in L^\infty(\Omega)\) and \(N_0, \Phi_0 \in L^\infty(\Omega) \cap H^1(\Omega)\), then \((T, N, \Phi)\) is called a weak-strong solution of problem (3.4)-(3.6) if \(T \in W_2\) and \(N, \Phi \in S_2\) and they satisfy

\[
\int_0^{T_f} (T_i, v)_{(H^1(\Omega), H_0^1(\Omega))} \ dt + \int_0^{T_f} \int_{\Omega} (\kappa_1 \ P (\Phi^K_+, T^K_+) + \kappa_0) \ \nabla T \cdot \nabla v \ dx \ dt = \int_0^{T_f} \int_{\Omega} f_1(T^K_+, N^C(T_+^+), \Phi^K_+) \ v \ dx \ dt,
\]

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\( \forall v \in L^2(0,T_f;H^1(\Omega)), \) the PDE system

\[
\begin{cases}
N_t - \epsilon \Delta N = f_2 \left( T^K_+, N^C(T_f)_+, \Phi^K_+ \right) & \text{a.e. in } (0,T_f) \times \Omega \\
\Phi_t - \epsilon \Delta \Phi = f_3 \left( T^K_+, N^C(T_f)_+, \Phi^K_+ \right)
\end{cases}
\]

and the boundary and initial conditions (3.5) and (3.6).

**Remark 3.2.** It is easy to prove for \( T \) and \( \Phi \) the estimates (3.3) following the same argument as in Lemma 3.1. For \( N \), the following differential inequality is satisfied

\[
\frac{\partial N}{\partial t} - \epsilon \Delta N \leq C_1 + C_2 N.
\]

Hence, \( N \leq \tilde{N} \) where \( \tilde{N} \) is the solution of the ODE equation

\[
\frac{\partial \tilde{N}}{\partial t} = C_1 + C_2 \tilde{N}.
\]

Thus, any solution of (3.4)-(3.6) satisfies that

\[
0 \leq T, \Phi \leq K, \quad 0 \leq N \leq C(T_f), \quad \text{a.e. in } (0,T_f) \times \Omega.
\]

**Theorem 3.2** (Existence of weak-strong solution of (3.4)-(3.6)). There exists a weak-strong solution \( (T,N,\Phi) \) of system (3.4)-(3.6) in the sense of Definition 3.2.

**Proof of Theorem 3.2**

We define the following operator

\[
R : \left( L^2(0,T_f;L^2(\Omega)) \right)^3 \rightarrow \left( L^2(0,T_f;L^2(\Omega)) \right)^3
\]

\[
\begin{pmatrix} \tilde{T}, \tilde{N}, \tilde{\Phi} \end{pmatrix} \rightarrow \begin{pmatrix} T, N, \Phi \end{pmatrix} = R \begin{pmatrix} \tilde{T}, \tilde{N}, \tilde{\Phi} \end{pmatrix}
\]

where \( (T,N,\Phi) \) is the weak-strong solution of the linear and decoupled problem

\[
\begin{cases}
\frac{\partial T}{\partial t} - \nabla \cdot \left( \left( \kappa_1 P \left( \Phi^K_+ , \tilde{\Phi}_+^K \right) + \kappa_0 \right) \nabla T \right) = f_1 \left( \tilde{T}_+^K , \tilde{N}_+^C(T_f) , \tilde{\Phi}_+^K \right) \\
\frac{\partial N}{\partial t} - \epsilon \Delta N = f_2 \left( \tilde{T}_+^K , \tilde{N}_+^C(T_f) , \tilde{\Phi}_+^K \right) \\
\frac{\partial \Phi}{\partial t} - \epsilon \Delta \Phi = f_3 \left( \tilde{T}_+^K , \tilde{N}_+^C(T_f) , \tilde{\Phi}_+^K \right)
\end{cases}
\]

subject to (3.5) and (3.6). Observe that thanks to (3.3), a weak-strong solution of (3.4)-(3.6) is a fixed point of \( R \). Therefore, we look for a fixed point of \( R \) using Leray-Schauder’s theorem 2.2.

**Lemma 3.2.** The operator \( R \) is well defined from \( (L^2(0,T_f;L^2(\Omega)))^3 \) to itself.

**Proof.** Using (1.6),

\[
0 \leq P \left( \Phi(t,x) \right)^K_+ \leq 1, \quad \text{a.e. } (t,x) \in (0,T_f) \times \Omega.
\]

On the other hand, one has

\[
\left\| f_i \left( \tilde{T}_+^K , \tilde{N}_+^C(T_f) , \tilde{\Phi}_+^K \right) \right\|_{L^\infty(0,T_f;L^\infty(\Omega))} \leq C_i \; \forall \; i = 1, 2, 3,
\]

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with $C_i$ independent of $\tilde{T}$, $\tilde{N}$ and $\tilde{\Phi}$. Hence, we can apply Theorem 2.1 to conclude that there exists a unique weak solution of (3.9) with the following regularity

$$(T, N, \Phi) \in \mathcal{W}_2 \times \mathcal{S}_2 \times \mathcal{S}_2.$$  

In particular,

$$(T, N, \Phi) \in \left( L^2 \left( 0, T_f; L^2 (\Omega) \right) \right)^3.$$  

\[\square\]

**Lemma 3.3.** The operator $\mathbf{R}$ is compact from $\left( L^2 \left( 0, T_f; L^2 (\Omega) \right) \right)^3$ to itself.

**Proof.** Let $\left( \tilde{T}, \tilde{N}, \tilde{\Phi} \right) \in \left( L^2 \left( 0, T_f; L^2 (\Omega) \right) \right)^3$. Then, applying the same argument of Lemma 3.2 and estimates (3.10) and (3.11), we prove that there exists a unique $(T, N, \Phi) = \mathbf{R} \left( \tilde{T}, \tilde{N}, \tilde{\Phi} \right)$ such that $(T, N, \Phi)$ is solution of (3.9) with the following estimates:

$$\left\| T \right\|_{\mathcal{W}_2} \leq C \left( \left\| T_0 \right\|_{L^2(\Omega)} , K , C \left( T_f \right) \right),$$

$$\left\| N \right\|_{\mathcal{S}_2} \leq C \left( \left\| N_0 \right\|_{L^2(\Omega)} , K , C \left( T_f \right) \right),$$

$$\left\| \Phi \right\|_{\mathcal{S}_2} \leq C \left( \left\| \Phi_0 \right\|_{L^2(\Omega)} , K , C \left( T_f \right) \right).$$

(3.12)

Hence, $(T, N, \Phi)$ is bounded in $\mathcal{W}_2 \times \mathcal{S}_2 \times \mathcal{S}_2$. Applying Aubin-Lions Theorem, we conclude that the embedding

$$\mathcal{W}_2 \times \mathcal{S}_2 \times \mathcal{S}_2 \hookrightarrow \left( L^2 \left( 0, T_f; L^2 (\Omega) \right) \right)^3$$

is compact. Thus, $\mathbf{R}$ is compact from $\left( L^2 \left( 0, T_f; L^2 (\Omega) \right) \right)^3$ to itself.  

\[\square\]

**Lemma 3.4.** The operator $\mathbf{R} : \left( L^2 \left( 0, T_f; L^2 (\Omega) \right) \right)^3 \longrightarrow \left( L^2 \left( 0, T_f; L^2 (\Omega) \right) \right)^3$ is continuous.

**Proof.** Given

$$\left( \tilde{T}_n, \tilde{N}_n, \tilde{\Phi}_n \right) \mapsto \left( \tilde{T}, \tilde{N}, \tilde{\Phi} \right) \in \left( L^2 \left( (0, T_f) ; L^2 (\Omega) \right) \right)^3,$$

(3.13)

we are going to check that

$$(T_n, N_n, \Phi_n) := \mathbf{R} \left( \tilde{T}_n, \tilde{N}_n, \tilde{\Phi}_n \right) \mapsto \mathbf{R} \left( \tilde{T}, \tilde{N}, \tilde{\Phi} \right) := (T, N, \Phi) \text{ in } \left( L^2 \left( (0, T_f) ; L^2 (\Omega) \right) \right)^3.$$  

Since $(T_n, N_n, \Phi_n) = \mathbf{R} \left( \tilde{T}_n, \tilde{N}_n, \tilde{\Phi}_n \right)$ is solution of (3.9), from (3.12) we obtain that $(T_n, N_n, \Phi_n)$ is bounded in $\mathcal{W}_2 \times \mathcal{S}_2 \times \mathcal{S}_2$. By Aubin-Lions Theorem the embeddings $\mathcal{W}_2 \hookrightarrow L^2 \left( 0, T_f ; L^2 (\Omega) \right)$ and $\mathcal{S}_2 \hookrightarrow L^2 \left( 0, T_f ; H^1 (\Omega) \right)$ are compact, hence there exists a subsequence $(T_{n_k}, N_{n_k}, \Phi_{n_k}) \in \mathcal{W}_2 \times \mathcal{S}_2 \times \mathcal{S}_2$ and a limit $(T^*, N^*, \Phi^*) \in \mathcal{W}_2 \times \mathcal{S}_2 \times \mathcal{S}_2$ such that

$$R \left( \tilde{T}_{n_k} , \tilde{N}_{n_k} , \tilde{\Phi}_{n_k} \right) \rightharpoonup_{k \to \infty} \left( T^*, N^* , \Phi^* \right) \text{ weakly in } \mathcal{W}_2 \times \mathcal{S}_2 \times \mathcal{S}_2,$$

$$R \left( \tilde{T}_{n_k} , \tilde{N}_{n_k} , \tilde{\Phi}_{n_k} \right) \rightharpoonup_{k \to \infty} \left( T^*, N^* , \Phi^* \right) \text{ strongly in } \left( L^2 \left( 0, T_f ; L^2 (\Omega) \right) \right)^3$$

and

$$(N_{n_k}, \Phi_{n_k}) \rightharpoonup_{k \to \infty} (N^*, \Phi^*) \text{ strongly in } \left( L^2 \left( 0, T_f ; H^1 (\Omega) \right) \right)^2.$$  

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In particular, 
\[(T_{n_k})_t, (N_{n_k})_t, (\Phi_{n_k})_t) \xrightarrow{k \to \infty} ((T^*)_t, (N^*)_t, (\Phi^*)_t) \quad \text{weakly in } \left( L^2 (0, T_f; (H^1 (\Omega))) \right)^3, \]
\[((N_{n_k})_t, (\Phi_{n_k})_t) \xrightarrow{k \to \infty} ((N^*)_t, (\Phi^*)_t) \quad \text{weakly in } (L^2 (0, T_f; L^2 (\Omega)))^2, \]
and
\[(\nabla T_{n_k}, \nabla N_{n_k}, \nabla \Phi_{n_k}) \xrightarrow{k \to \infty} (\nabla T^*, \nabla N^*, \nabla \Phi^*) \quad \text{weakly in } (L^2 (0, T_f; L^2 (\Omega)))^3. \]

Using the pointwise convergence
\[
\left( \tilde{T}_n (t, x), \tilde{N}_n (t, x), \tilde{\Phi}_n (t, x) \right) \rightarrow \left( \tilde{T} (t, x), \tilde{N} (t, x), \tilde{\Phi} (t, x) \right), \quad \text{a.e. } (t, x) \in (0, T_f) \times \Omega
\]
one also has
\[
\left( (\tilde{T}_n (t, x))^+_C, (\tilde{N}_n (t, x))^+_C, (\tilde{\Phi}_n (t, x))^+_C \right) \rightarrow \left( (\tilde{T} (t, x))^+_C, (\tilde{N} (t, x))^+_C, (\tilde{\Phi} (t, x))^+_C \right)
\]
a.e. \((t, x) \in (0, T_f) \times \Omega\).

Since \[\|P \left( \tilde{\Phi}^+_K, \tilde{T}^+_K \right) \|_{L^\infty (0, T_f; L^\infty (\Omega))} \leq 1 \text{ and } P \left( \tilde{\Phi}, \tilde{T} \right) \text{ is continuous in } \mathbb{R}^2, \]
applying dominated convergence Theorem, we can deduce that
\[
P \left( (\tilde{\Phi}_{n_k})^+_K, (\tilde{T}_{n_k})^+_K \right) \xrightarrow{k \to \infty} P \left( \tilde{\Phi}^+_K, \tilde{T}^+_K \right) \quad \text{in } L^p (0, T_f; L^p (\Omega)), \quad \forall p < \infty. \tag{3.14}
\]

Since \[\|f_i \left( \tilde{T}^+_K, \tilde{N}^+_C (T^i), \tilde{\Phi}^+_K \right) \|_{L^\infty (0, T_f; L^\infty (\Omega))} \leq C \text{ and } \tag{3.13} \]
applying dominated convergence Theorem, we deduce that
\[
f_i \left( (\tilde{T}_{n_k})^+_K, (\tilde{N}_{n_k})^+_C (T^i), (\tilde{\Phi}_{n_k})^+_K \right) \xrightarrow{k \to \infty} f_i \left( \tilde{T}^+_K, \tilde{N}^+_C (T^i), \tilde{\Phi}^+_K \right)
\]
in \(L^p (0, T_f; L^p (\Omega))\) for all \(p < \infty\) and for \(i = 1, 2, 3\).

On the other hand, \(\nabla T_{n_k} \xrightarrow{k \to \infty} \nabla T^* \) weakly in \(L^2 (0, T_f; L^2 (\Omega))\). Thus, we obtain
\[
P \left( (\tilde{\Phi}_{n_k})^+_K, (\tilde{T}_{n_k})^+_K \right) \nabla T_{n_k} \quad \text{is bounded in } L^2 (0, T_f; L^2 (\Omega)). \quad \text{Consequently,}
\]
\[
P \left( (\tilde{\Phi}_{n_k})^+_K, (\tilde{T}_{n_k})^+_K \right) \nabla T_{n_k} \xrightarrow{k \to \infty} P \left( \tilde{\Phi}^+_K, \tilde{T}^+_K \right) \nabla T^* \quad \text{weakly in } (L^2 (0, T_f; L^2 (\Omega)))^3.
\]

Thus, passing to the limit in the problem satisfied by \((T_{n_k}, N_{n_k}, \Phi_{n_k})\), we have that \((T^*, N^*, \Phi^*) = \mathbf{R} \left( \tilde{T}, \tilde{N}, \tilde{\Phi} \right) \) and since the solution \(\mathbf{R} \left( \tilde{T}, \tilde{N}, \tilde{\Phi} \right) \) of \([4.9] \) is unique, we conclude the convergence of the whole sequence, that is,
\[
\mathbf{R} \left( \tilde{T}_n, \tilde{N}_n, \tilde{\Phi}_n \right) = (T_n, N_n, \Phi_n) \rightarrow \mathbf{R} \left( \tilde{T}, \tilde{N}, \tilde{\Phi} \right) = (T, N, \Phi) \quad \text{in } (L^2 (0, T_f; L^2 (\Omega)))^3.
\]

Now we introduce a notation for vectorial norms. Given a space \(X\) and \(f, g, h \in X\),
\[
\|f, g, h\|_X^2 = \|f\|_X^2 + \|g\|_X^2 + \|h\|_X^2.
\]
**Lemma 3.5.** If \((T, N, \Phi) = \lambda R(T, N, \Phi)\) for some \(\lambda \in [0, 1]\), then
\[
\|T, N, \Phi\|_{L^2(0, T_f; L^2(\Omega))} \leq C
\]
with \(C > 0\) independent of \(\lambda \in [0, 1]\).

*Proof.* For \(\lambda = 0\) is trivial, hence we suppose \(\lambda \in (0, 1]\). Let \((T, N, \Phi) \in L^2 \left(0, T_f; L^2(\Omega)\right)\) such that \((T, N, \Phi) = \lambda R(T, N, \Phi)\). Then \((T, N, \Phi)\) is solution of a system similar to \((3.4) - (3.6)\) with \(\lambda\) multiplying in the right hand side. Therefore, we can follow the same argument that in Lemma 3.1 to obtain that \(0 \leq T, \Phi \leq K\) and \(0 \leq N \leq C(T_f)\) a.e. \((0, T_f) \times \Omega\).

Thus, \((T, N, \Phi)\) is bounded in \((L^\infty(0, T_f; L^\infty(\Omega)))^3\) and also in \((L^2(0, T_f; L^2(\Omega)))^3\) independently of \(\lambda \in [0, 1]\).

Finally, from Lemmas 3.3, 3.4 and 3.5 the operator \(R\) satisfies the hypotheses of Theorem 2.2.

Thus, we conclude that the map \(R\) has a fixed point \((T_e, N_e, \Phi_e)\) which is a weak-strong solution of problem \((3.4)-(3.6)\).

**Step 2. \(\epsilon\)-independent estimates**

Once we have proved the existence of weak-strong solution for the regularized problem \((3.4)-(3.6)\), we are going to take \(\epsilon \to 0\) in order to obtain a weak-strong solution of problem \((3.2)\).

We can deduce the following \(\epsilon\) independent estimates for the solution \((T_e, N_e, \Phi_e)\):

- Following the proof of Lemma 3.1, we can obtain that
  \[
  0 \leq T_e, \Phi_e \leq K \quad \text{and} \quad 0 \leq N_e \leq C(T_f), \quad \text{a.e. in } (0, T_f) \times \Omega. \tag{3.15}
  \]

- Following the proof of Lemma 3.1 b) for the problems satisfied by \(N_e\) and \(\Phi_e\), we have the bounds
  \[
  \|N_e, \Phi_e\|^2_{L^\infty(0, T_f; L^2(\Omega))} + \|\nabla \left(\sqrt{\epsilon} N_e\right), \nabla \left(\sqrt{\epsilon} \Phi_e\right)\|^2_{L^2(0, T_f; L^2(\Omega))} \leq C \left(\|N_0, \Phi_0\|_{L^2(\Omega)}, |\Omega|, K, T_f\right).
  \]
  Hence,
  \[
  \left(\sqrt{\epsilon} \nabla N_e, \sqrt{\epsilon} \nabla \Phi_e\right) \text{ is bounded in } L^2 \left(0, T_f; L^2(\Omega)\right). \tag{3.16}
  \]

- From Lemma 3.1 b), we obtain that
  \[
  T_e \text{ is bounded in } L^\infty \left(0, T_f; L^2(\Omega)\right) \cap L^2 \left(0, T_f; H^1(\Omega)\right).
  \]

- From (3.16), we obtain the bounds
  \[
  \left(\sqrt{\epsilon} \Delta \Phi_e, \sqrt{\epsilon} \Delta N_e\right) \text{ in } L^2 \left(0, T_f; (H^1(\Omega))'\right). \tag{3.17}
  \]

- Moreover, from (3.4) we obtain that
  \[
  \begin{cases}
  (T_e)_t \text{ is bounded in } L^2 \left(0, T_f; (H^1(\Omega))'\right), \\
  (N_e)_t, (\Phi_e)_t \text{ are bounded in } L^\infty \left(0, T_f; L^\infty(\Omega)\right)
  \end{cases}
  \tag{3.18}
  \]
  because \(f_i \left(\left(\tilde{T}_{t_i}\right)^{K}_+, \left(\tilde{N}_{t_i}\right)^{C(T_f)}_+, \left(\tilde{\Phi}_{t_i}\right)^{K}_+\right)\) is bounded in \(L^\infty \left(0, T_f; L^\infty(\Omega)\right)\) for \(i = 1, 2, 3\).
We will see the following additional estimate.

**Lemma 3.6.** Assume $N_0, \Phi_0 \in H^1(\Omega)$, then $N_\epsilon, \Phi_\epsilon$ are bounded in $L^\infty\left(0, T_f; H^1(\Omega)\right)$.

**Proof.** We only make the proof for $N_\epsilon$ because for $\Phi_\epsilon$ is similar. Multiplying the $N_\epsilon$ equation by $-\Delta N_\epsilon \in L^2\left(0, T_f; L^2(\Omega)\right)$ and integrating in $\Omega$, we obtain

$$\frac{1}{2} \frac{d}{dt} \|\nabla N_\epsilon\|_{L^2(\Omega)}^2 + \epsilon \|\Delta N_\epsilon\|_{L^2(\Omega)}^2 \, dx = \int_\Omega f_2 \left((T_\epsilon)_+, (N_\epsilon)^{(T_f)}_+, (\Phi_\epsilon)^{(T_f)}_+\right) \left(-\Delta N_\epsilon\right) \, dx \tag{3.19}$$

where the right hand side of (3.19) after integrating by parts can be bounded as follows

$$\int_\Omega f_2 \left((T_\epsilon)_+, (N_\epsilon)^{(T_f)}_+, (\Phi_\epsilon)^{(T_f)}_+\right) \left(-\Delta N_\epsilon\right) \, dx \leq C \left(\|\nabla T_\epsilon \cdot \nabla N_\epsilon\|_{L^2(\Omega)} + \|\nabla N_\epsilon\|_{L^2(\Omega)}^2 \right) + 1 + \|\nabla T_\epsilon\|_{L^2(\Omega)}^2 \|\nabla N_\epsilon, \nabla \Phi_\epsilon\|_{L^2(\Omega)}^2. \tag{3.20}$$

Here, we have used that every partial derivative $\frac{\partial f_2}{\partial T}, \frac{\partial f_2}{\partial N}$ and $\frac{\partial f_2}{\partial \Phi}$ evaluated at $((T_\epsilon)_+, (N_\epsilon)^{(T_f)}_+, (\Phi_\epsilon)^{(T_f)}_+)$ is bounded in $L^\infty\left(0, T_f; L^\infty(\Omega)\right)$ and the fact that $|\nabla (T_\epsilon)_+| \leq |\nabla T_\epsilon|$ and the same for $\nabla (N_\epsilon)^{(T_f)}_+$ and $\nabla (\Phi_\epsilon)^{(T_f)}_+$. Taking into account this estimate in (3.19), we obtain that

$$\frac{1}{2} \frac{d}{dt} \|\nabla N_\epsilon, \nabla \Phi_\epsilon\|_{L^2(\Omega)}^2 + \epsilon \|\Delta N_\epsilon, \Delta \Phi_\epsilon\|_{L^2(\Omega)}^2 \leq C \left(1 + \|\nabla T_\epsilon\|_{L^2(\Omega)}^2\right) \|\nabla N_\epsilon, \nabla \Phi_\epsilon\|_{L^2(\Omega)}^2. \tag{3.21}$$

Since $\nabla T_\epsilon$ is bounded in $L^2\left(0, T_f; L^2(\Omega)\right)$, applying Gronwall Lemma, we deduce that

$$(\nabla N_\epsilon, \nabla \Phi_\epsilon) \text{ is bounded in } L^\infty\left(0, T_f; L^2(\Omega)\right).$$

Hence,

$$(N_\epsilon, \Phi_\epsilon) \text{ is bounded in } L^\infty\left(0, T_f; H^1(\Omega)\right).$$

Finally, integrating in time the inequality (3.21), we obtain the following bounds

$$\|\Delta (\sqrt{\epsilon} N_\epsilon) \cdot \Delta (\sqrt{\epsilon} \Phi_\epsilon)\|_{L^2(0,T_f;L^2(\Omega))}^2 \leq C.$$

Hence one has the bound of $(\sqrt{\epsilon} N_\epsilon, \sqrt{\epsilon} \Phi_\epsilon)$ in $L^2\left(0, T_f; H^2(\Omega)\right)$.

\[ \square \]

**Step 3. Taking limits as $\epsilon \to 0$**

Using (3.15), (3.16), (3.17), (3.18) and Lemma 3.1(b), we can conclude that there exists a subsequence $(T_\epsilon, N_\epsilon, \Phi_\epsilon) \in W_2$, with $N_\epsilon, \Phi_\epsilon \in L^\infty\left(0, T_f; H^1(\Omega)\right)$ and a limit $(T, N, \Phi)$ such that as $\epsilon \to 0$,

\[ \begin{align*}
T_\epsilon & \to T \quad \text{weakly in } W_2, \\
(N_\epsilon, \Phi_\epsilon) & \rightharpoonup (N, \Phi) \quad \text{weakly * in } L^\infty\left(0, T_f; H^1(\Omega)\right), \\
(T_\epsilon)_t & \to T_t \quad \text{weakly in } L^2\left(0, T_f; H^1(\Omega)\right), \\
((N_\epsilon)_t, (\Phi_\epsilon)_t) & \rightharpoonup (N_t, \Phi_t) \quad \text{weakly * in } L^\infty\left(0, T_f; L^\infty(\Omega)\right), \\
\nabla T_\epsilon & \to \nabla T \quad \text{weakly in } L^2\left(0, T_f; L^2(\Omega)\right), \\
(\sqrt{\epsilon} \Delta N_\epsilon, \sqrt{\epsilon} \Delta \Phi_\epsilon) & \to (\theta_1, \theta_2) \quad \text{weakly in } L^2\left(0, T_f; L^2(\Omega)\right).
\end{align*} \]
In particular, 
\[ (\epsilon \Delta N_\epsilon, \epsilon \Delta \Phi_\epsilon) = (\sqrt{\epsilon} (\sqrt{\epsilon} \Delta N_\epsilon), \sqrt{\epsilon} (\sqrt{\epsilon} \Delta \Phi_\epsilon)) \to (0, 0) \text{ weakly in } L^2 \blacksquare \]

From Aubin-Lions compactness 
\[
\begin{align*}
T_\epsilon & \to T \quad \text{strong in } L^2(0,T_f;L^2(\Omega)) \cap C^0(0,T_f;(H^1(\Omega))'), \\
(N_\epsilon, \Phi_\epsilon) & \to (N, \Phi) \quad \text{strong in } (C^0(0,T_f;L^2(\Omega)))^2.
\end{align*}
\] 

(3.22)

Now, we will take limits in the nonlinear diffusion term in \( L^2(0,T_f;L^2(\Omega)) \). On the one hand, we have that \( \kappa_1 \mathcal{P} (\Phi_\epsilon, T_\epsilon) + \kappa_0 \) is continuous in \( \mathbb{R}^2 \) and it is bounded in \( L^\infty(0,T_f,L^\infty(\Omega)) \) and for \( L^p \), we obtain that \( (T_\epsilon, \Phi_\epsilon) \to (T, \Phi) \) a.e. in \( (0,T_f) \times \Omega \). Hence, using dominated convergence Theorem

\[
\left( \kappa_1 \mathcal{P} \left( (\Phi_\epsilon)_+^K, (T_\epsilon)_+^K \right) + \kappa_0 \right) \to \left( \kappa_1 \mathcal{P} \left( (\Phi)_+^K, (T)_+^K \right) + \kappa_0 \right) \quad \text{in } L^p \left( 0, T_f; L^p(\Omega) \right), \quad \forall p < \infty.
\]

(3.23)

On the other hand, \( \nabla T_\epsilon \to \nabla T \) weakly in \( L^2(0,T_f;L^2(\Omega)) \).

Hence, since \( \left( \kappa_1 \mathcal{P} \left( (\Phi_\epsilon)_+^K, (T_\epsilon)_+^K \right) + \kappa_0 \right) \nabla T_\epsilon \) is bounded in \( L^2(0,T_f;L^2(\Omega)) \), one has

\[
\left( \kappa_1 \mathcal{P} \left( (\Phi_\epsilon)_+^K, (T_\epsilon)_+^K \right) + \kappa_0 \right) \nabla T_\epsilon \to \left( \kappa_1 \mathcal{P} \left( (\Phi)_+^K, (T)_+^K \right) + \kappa_0 \right) \nabla T \quad \text{weakly in } L^2(0,T_f;L^2(\Omega)).
\]

Finally, for all \( \varphi \in L^2 \left( 0, T_f; H^1(\Omega) \right) \) we conclude that

\[
\int_0^{T_f} \int_\Omega \left( (T_\epsilon)_1, (N_\epsilon)_1, (\Phi_\epsilon)_1 \right) \varphi \, dx \, dt \to \int_0^{T_f} \int_\Omega \left( T_1, N_1, \Phi_1 \right) \varphi \, dx \, dt,
\]

\[
\int_0^{T_f} \int_\Omega \left( \kappa_1 \mathcal{P} \left( (\Phi_\epsilon)_+^K, (T_\epsilon)_+^K \right) + \kappa_0 \right) \nabla T_\epsilon \cdot \nabla \varphi \, dx \, dt \to \int_0^{T_f} \int_\Omega \left( \kappa_1 \mathcal{P} \left( (\Phi)_+^K, (T)_+^K \right) + \kappa_0 \right) \nabla T \cdot \nabla \varphi \, dx \, dt,
\]

\[
\int_0^{T_f} \int_\Omega \left( \sqrt{\epsilon} (\sqrt{\epsilon} \Delta N_\epsilon), \sqrt{\epsilon} (\sqrt{\epsilon} \Delta \Phi_\epsilon) \right) \varphi \, dx \, dt \to (0,0),
\]

\[
\int_0^{T_f} \int_\Omega f_i \left( (T_\epsilon)_+, (N_\epsilon)_+, (\Phi_\epsilon)_+ \right) \varphi \, dx \, dt \to \int_0^{T_f} \int_\Omega f_i \left( T_+, N_+, \Phi_+ \right) \varphi \, dx \, dt,
\]

para \( i = 1, 2, 3. \)

Taking limits as \( \epsilon \to 0 \) in \( [3.9] \), we deduce that \( (T, N, \Phi) \) is a weak-strong solution of \( [3.2] \) (which is in addition a weak-strong solution of problem \( [1.1]-[1.3] \)) where the convergence for \( [1.3] \) is obtained thanks to \( [3.22] \). \( \square \)

4 Asymptotic behaviour

Once we have proved the existence of weak-strong solution of \( [1.1]-[1.3] \) for any finite time \( T_f > 0 \), we are going to study the asymptotic behaviour of the solution as \( t \to \infty \). In order to obtain the equilibrium points, we solve the following nonlinear algebraic system

\[
f_1 \left( T, N, \Phi \right) = 0, \quad f_2 \left( T, N, \Phi \right) = 0, \quad f_3 \left( T, N, \Phi \right) = 0.
\]

Following the same argument used in [11 Section 4.1], the equilibria of \( [1.1] \) are

- \( P_1 = \{(0,0,0)\} \).
- \( P_2 = \{(0,N,0), \quad N > 0\} \),
- \( P_3 = \{(0,0,\Phi), \quad \Phi > 0\} \).

(4.1)
Remark 4.1. Observe that $P_1 \cup P_2 \cup P_3$ is a continuum of equilibria points.

Remark 4.2. In the following results, we assume sometimes the hypothesis $N_0(x) > 0$ for $x \in \overline{\Omega}$. However, this condition can be relaxed for $N(t_*, x)$ for some $t_* \geq 0$, by considering the problem starting in $t = t_*$.

Now, we present a result of pointwise convergence to zero of the vasculature.

**Lemma 4.1.** Given $\epsilon > 0$ and a solution $(T, N, \Phi)$ of (4.1)-(4.3), if there exists $\tilde{\Omega} \subset \Omega$ with $|\tilde{\Omega}| > 0$ such that $0 < \epsilon \leq N_0(x)$ a.e. $x \in \tilde{\Omega}$, one has $\Phi(t, x) \to 0$ when $t \to +\infty$ a.e. $x \in \tilde{\Omega}$.

The proof of this result is rather similar to [11, Lemma 12] with the difference that due to the fact that $\Phi(t, x), N(t, x) \in L^\infty(0, T_f; H^1(\Omega))$, we prove Lemma 4.1 using a subdomain $\tilde{\Omega} \subset \Omega$ with positive measure instead of a pointwise argument for every $x \in \Omega$.

As consequence of Lemma 4.1 and that $t \mapsto N(t, \cdot)$ is increasingly a.e. $x \in \Omega$, we deduce:

**Corollary 4.1.** The equilibria solution $P_3$ is unstable.

Now, we prove a comparison result that provides a uniform bound for the solution of a nonlinear diffusion equation which we will use later:

**Lemma 4.2.** Let $\Omega \subseteq \mathbb{R}^n$ a bounded set of class $C^2$, and $0 < T_f < +\infty$. Given the following problems

\[
\begin{cases}
T_t - \nabla (\nu (t, x, T) \cdot \nabla T) = f(t, x, T) \quad \text{in} \quad (0, T_f) \times \Omega, \\
T(0, x) = T_0(x) \quad \text{in} \quad \Omega, \\
\frac{\partial T}{\partial n} = 0 \quad \text{in} \quad (0, T_f) \times \partial \Omega,
\end{cases}
\]

with $\nu (\cdot, \cdot, T) \in L^\infty(0, T_f; L^\infty(\Omega)) \ \forall \ T \in \mathbb{R}$ a given non-negative function and $f(\cdot, \cdot, T) \in L^2(0, T_f; H^1(\Omega)) \ \forall \ T \in \mathbb{R}$ and

\[
\begin{cases}
y_t = g(t, y) \quad \text{in} \quad (0, T_{\text{max}}), \\
y(0) = y_0
\end{cases}
\]

with $0 < T_{\text{max}} < +\infty$ and $g \in C^0(0, T_{\text{max}}) \times \mathbb{R}$ and locally lipschitz with respect $y$. Suppose that (4.2) has a weak solution $T \in W_2 \cap L^\infty(0, T_f; L^\infty(\Omega))$ in $(0, T_f) \times \Omega$, and (4.3) has a unique solution $y \in C^1([0, T_{\text{max}}])$ in $[0, T_{\text{max}}]$. If $T_0(x) \leq y_0$ a.e. $x \in \Omega$ and

\[
f(t, x, p) \leq g(t, p), \quad \text{a.e.} \quad (t, x) \in (0, T_*) \times \Omega, \quad \forall \ p \in \mathbb{R}
\]

with $T_* = \min \{T_f, T_{\text{max}}\}$. Then,

\[
T(t, x) \leq y(t), \quad \text{a.e.} \quad (t, x) \in (0, T_*) \times \Omega.
\]

**Proof.** Let $T = T(t, x)$ a weak solution of (4.2) in $(0, T_f)$ and $y = y(t)$ the classical solution of (4.3) in $[0, T_{\text{max}}]$ and we consider the problem which satisfies the difference $T - y$,

\[
\begin{cases}
(T - y)_t - \nabla \cdot (\nu (t, x, T) \nabla (T - y)) = f(t, x, T) - g(t, y) \quad \text{in} \quad (0, T_*) \times \Omega, \\
T(0, x) - y(0) = T_0(x) - y_0 \quad \text{a.e.} \quad x \in \Omega, \\
\frac{\partial (T - y)}{\partial n} = 0 \quad \text{in} \quad (0, T^*) \times \partial \Omega,
\end{cases}
\]

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To prove the theorem, we repeat the same argument for the exponential convergence of \( \Phi(t, x) \) to zero in \( L^\infty(0, T_f; L^\infty(\Omega)) \) made in [11, Lemma 13]. To prove (4.7), we bound \( f_1(T, N, \Phi) \) using (4.6) as follows

\[
f_1(T, N, \Phi) \leq \rho \| \Phi_0 \|_{L^\infty(\Omega)} e^{-\beta_2 N_0^{\min} t} - \beta_1 N_0^{\min} T,
\]

and we apply Lemma 4.2 taking the following linear differential problem

\[
\begin{align*}
y_t &= \rho \| \Phi_0 \|_{L^\infty(\Omega)} e^{-\beta_2 N_0^{\min} t} - \beta_1 N_0^{\min} y, \quad 0 \leq t < \infty, \\
y(0) &= \| T_0 \|_{L^\infty(\Omega)}.
\end{align*}
\]

Multiplying the first equation of (4.5) by \( (T - y)_+ \) and integrating in \( \Omega \) and using (4.4), we obtain that

\[
\frac{1}{2} \frac{d}{dt} \int_\Omega (T - y)_+^2 \, dx + \int_\Omega \nu(t, x, T) |\nabla (T - y)_+^2 | \, dx = \int_\Omega (f(t, x, T) - g(t, y))(T - y)_+ \, dx \leq \int_\Omega (g(t, T) - g(t, y))(T - y)_+ \, dx \leq L_R \int_\Omega (T - y)_+^2 \, dx
\]

since the graph of \( T(t, x) \) and \( y(t) \) belong to a compact set \( \tilde{K} \subset \mathbb{R} \) because \( T \in L^\infty(0, T_f; L^\infty(\Omega)) \) and \( y \in C^1([0, T_{\text{max}}]) \) and hence \( L_R \) is a Lipschitz constant of this compact set. Thus, we deduce

\[
\| (T - y)_+ \|_{L^2(\Omega)}^2 \leq \| (T_0(x) - y_0)_+ \|_{L^2(\Omega)}^2 e^{2L_R t} = 0,
\]

hence, \( T(t, x) \leq y(t) \) a.e. \( (t, x) \in (0, T_\ast) \times \Omega \).

Now, using Lemma 4.2 we are going to deduce the same results for the asymptotic behaviour of any solution \( (T, N, \Phi) \) of (1.1)-(1.3) which we proved in [11, Lemmas 13 and 15], where uniform convergence for \( (T, N, \Phi) \) was obtained.

**Lemma 4.3.** Given a solution \( (T, N, \Phi) \) of (1.1)-(1.3) such that

\[
N_0(x) \geq N_0^{\min} > 0 \quad \text{a.e.} \quad x \in \Omega
\]

and assume that

\[
\delta \geq \frac{\gamma}{K}, \quad (4.6)
\]

Then,

\[
0 \leq \Phi(t, x) \leq \| \Phi_0 \|_{L^\infty(\Omega)} e^{-\beta_2 N_0^{\min} t}, \quad \text{a.e.} \quad (t, x) \in (0, +\infty) \times \Omega. \quad (4.7)
\]

In addition, it holds that if \( \beta_1 \neq \beta_2 \), then

\[
0 \leq T(t, x) \leq \| T_0 \|_{L^\infty(\Omega)} e^{-\beta_1 N_0^{\min} t} + \frac{\rho \| \Phi_0 \|_{L^\infty(\Omega)}}{\beta_1 - \beta_2} N_0^{\min} \left( e^{-\beta_2 N_0^{\min} t} - e^{-\beta_1 N_0^{\min} t} \right), \quad \text{a.e.} \quad (t, x) \in (0, +\infty) \times \Omega, \quad (4.8)
\]

whereas if \( \beta_1 = \beta_2 \), then

\[
0 \leq T(t, x) \leq (\| T_0 \|_{L^\infty(\Omega)} + \rho \| \Phi_0 \|_{L^\infty(\Omega)} t) e^{-\beta_1 N_0^{\min} t}, \quad \text{a.e.} \quad (t, x) \in (0, +\infty) \times \Omega. \quad (4.9)
\]

Moreover, there exists \( N_{\text{max}} > \| N_0 \|_{L^\infty(\Omega)} \) such that

\[
N(t, x) \leq N_{\text{max}}, \quad \text{a.e.} \quad (t, x) \in (0, +\infty) \times \Omega.
\]

**Proof.** To prove (4.7) we repeat the same argument for the exponential convergence of \( \Phi(t, x) \) to zero.
Solving (4.10) we obtain that if $\beta_1 \neq \beta_2$,
\[ y(t) = \| T_0 \|_{L^\infty(\Omega)} e^{-\beta_1 N_0^\text{min} t} + \frac{\rho \| \Phi_0 \|_{L^\infty(\Omega)}}{\beta_1 - \beta_2} N_0^\text{min} (e^{-\beta_2 N_0^\text{min} t} - e^{-\beta_1 N_0^\text{min} t}), \quad \text{in } (0, +\infty), \]
and if $\beta_1 = \beta_2$,
\[ y(t) = (\| T_0 \|_{L^\infty(\Omega)} + \rho \| \Phi_0 \|_{L^\infty(\Omega)} t) e^{-\beta_1 N_0^\text{min} t}, \quad \text{in } (0, +\infty). \]

Hence, we obtain that
\[ T(t, x) \leq y(t), \quad \text{a.e. } (t, x) \in (0, +\infty) \times \Omega. \]

Finally, we get the bound $N(t, x) \leq N_{\text{max}}$ as in [11, Lemma 13] using the upper uniform bounds obtained for $T(t, x)$ and $\Phi(t, x)$ previously in [4.7] and [4.8] or [4.9]. \qed

In the following result, we study the situation when $N_0(x)$ is close to $K$ in the whole domain $\Omega$.

**Lemma 4.4.** Assuming $N_0(x) \geq K - \epsilon$ a.e. $x \in \Omega$ for $\epsilon$ small enough and a weak-strong solution $(T, N, \Phi)$ of (1.1)-(1.3), then,

\[ 0 \leq T(t, x) \leq \| T_0 \|_{L^\infty(\Omega)} e^{-\left(\beta_1(K-\epsilon) - \rho \frac{\epsilon}{K}\right) t}, \quad \text{a.e. } (t, x) \in (0, +\infty) \times \Omega, \quad (4.11) \]

and

\[ 0 \leq \Phi(t, x) \leq \| \Phi_0 \|_{L^\infty(\Omega)} e^{-\left(\beta_2(K-\epsilon) - \gamma \frac{\epsilon}{K}\right) t}, \quad \text{a.e. } (t, x) \in (0, +\infty) \times \Omega, \quad (4.12) \]

In addition, if $\rho \frac{\epsilon}{K} - \beta_1 (K - \epsilon) < 0$ and $\gamma \frac{\epsilon}{K} - \beta_2 (K - \epsilon) < 0$ then, there exists $N_{\text{max}} > \| N_0 \|_{L^\infty(\Omega)}$ such that

\[ N(t, x) \leq N_{\text{max}}, \quad \text{a.e. } (t, x) \in (0, +\infty) \times \Omega. \quad (4.13) \]

**Proof.** Since $N$ is increasing in time, we get

\[ N(t, x) \geq N_0(x) > K - \epsilon \quad \text{a.e. } (t, x) \in (0, +\infty) \times \Omega. \]

Using now that $T, \Phi \geq 0$, and

\[ 1 - \frac{T + N + \Phi}{K} \leq 1 - \frac{N}{K} < 1 - \frac{K - \epsilon}{K} = \frac{\epsilon}{K}, \]

therefore,

\[ \frac{\partial T}{\partial t} - \nabla \cdot ((\kappa_1 P(\Phi, T) + \kappa_0) \nabla T) = f_1(T, N, \Phi) \leq \rho \frac{\epsilon}{K} - \beta_1 (K - \epsilon) T = \left(\rho \frac{\epsilon}{K} - \beta_1 (K - \epsilon)\right) T. \]

Hence, we apply Lemma 4.2 with $y_0 = \| T_0 \|_{L^\infty(\Omega)}$ and $g(t, y) = \left(\rho \frac{\epsilon}{K} - \beta_1 (K - \epsilon)\right) y$ to obtain that

\[ T(t, x) \leq y(t) = \| T_0 \|_{L^\infty(\Omega)} e^{-\left(\beta_1(K-\epsilon) - \rho \frac{\epsilon}{K}\right) t}, \quad \text{a.e. } (t, x) \in (0, +\infty) \times \Omega. \]

Now we repeat the same argument made in [11, Lemma 15] to prove the uniform exponential convergence of $\Phi(t, x)$ to zero in $L^\infty(0, T_f; L^\infty(\Omega))$ given in (4.12) and for the bound of $N(t, x)$ given in (4.13) using the upper uniform bounds (4.11) and (4.12) already proved for $T(t, x)$ and $\Phi(t, x)$. \qed

**Remark 4.3.** In Lemmas 4.3 and 4.4 using that $N(\cdot, x)$ is increasing in time, there exists $N_\ast \in L^\infty(\Omega)$ with $N_{\text{max}} \geq N_\ast \geq N_0$ a.e. in $\Omega$ such that

\[ N(t, x) \to N_\ast(x) \quad \text{as } t \to +\infty, \quad \text{a.e. } x \in \Omega. \]
5 A FE numerical scheme

In this part, we build an uncoupled and linear fully discrete scheme of \((1.1) - (1.3)\) by means of a Implicit-Explicit (IMEX) Finite Difference in time approximation and \(P_1\) continuous finite element with "mass-lumping" in space. This scheme will preserve the pointwise and energy estimates that appear in Lemmas \([3.1]\) and \([3.6]\) considering acute triangulations. In a forthcoming paper, we will use this numerical scheme to show simulations related to different kinds of glioblastoma growth.

Now we introduce the hypotheses required along this section.

a) Let \(0 < T_f < +\infty\) and a bounded set \(\Omega \subseteq \mathbb{R}^2\) or \(\mathbb{R}^3\) with polygonal or polyhedral lipschitz-continuous boundary. We consider the uniform time partition

\[
(0, T_f) = \bigcup_{k=0}^{K_f-1} (t_k, t_{k+1}],
\]

with \(t_k = k dt\) where \(K_f \in \mathbb{N}\) and \(dt = \frac{T_f}{K_f}\) is the time step.

b) Let \(\{T_h\}_{h>0}\) be a family of shape-regular, quasi-uniform triangulations of \(\Omega\) formed by acute \(N\)-simplexes (triangles in 2D and tetrahedral in 3D), such that

\[
\Omega = \bigcup_{K \in T_h} K,
\]

where \(h = \max_{K \in T_h} h_K\), with \(h_K\) being the diameter of \(K\). Further, let \(N_h = \{a_i\}_{i \in I} \) be the set of all the nodes of \(T_h\).

c) Conforming piecewise linear, finite element spaces associated to \(T_h\) are assumed for approximating \(H^1(\Omega)\):

\[
N_h = \{ n_h \in C^0(\Omega) : \ n_h|_K \in P_1(K) \ \forall K \in T_h \}
\]

whose Lagrange basis is denoted by \(\{\varphi_a\}_{a \in N_h}\).

Let \(I_h : C^0(\Omega) \to N_h\) be the nodal interpolation operator and consider the discrete inner product

\[
(n_h, n_h)_h = \int_\Omega I_h (n_h \cdot n_h) = \sum_{a \in N_h} n_h(a) \ n_h(a) \int_\Omega \varphi_a, \ \forall n_h, n_h \in N_h
\]

which induces the discrete norm \(\|n_h\|_h = \sqrt{(n_h, n_h)_h}\) defined on \(N_h\) (that is equivalent to \(L^2(\Omega)\)-norm). Thus, in each time step, we consider the following linear uncoupled numerical scheme for the model \([1.1]\): given \(T_h^k, N_h^k, \Phi_h^k \in N_h\), find \(T_h^{k+1}, N_h^{k+1}, \Phi_h^{k+1} \in N_h\) in a decoupled way (first \(T\), then \(\Phi\) and finally \(N\)) satisfying

\[
\left( \delta_t T_h^{k+1}, v \right)_h + \left( (\kappa_1 P(\Phi_h^k T_h^k) + \kappa_0) \nabla T_h^{k+1}, \nabla v \right)_h = \left( \hat{f}_1 \left( T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k \right), v \right)_h \tag{5.1}
\]

\[
\delta_t N_h^{k+1}(a) = \hat{f}_2 \left( T_h^k(a), T_h^{k+1}(a), N_h^k(a), \Phi_h^k(a), \Phi_h^{k+1}(a) \right) \tag{5.2}
\]

\[
\delta_t \Phi_h^{k+1}(a) = \hat{f}_3 \left( T_h^k(a), T_h^{k+1}(a), N_h^k(a), \Phi_h^k(a), \Phi_h^{k+1}(a) \right) \tag{5.3}
\]

\(\forall v \in N_h\) and \(\forall a \in N_h\). We have denoted

\[
\delta_t T_h^{k+1} = \frac{T_h^{k+1} - T_h^k}{dt}
\]
and similarly for $\delta_t N_h^{k+1}$ and $\delta_t \Phi_h^{k+1}$. The approximation of the initial conditions are taken as

$$T_h^0 = I_h(T_0) \in N_h, \ N_h^0 = I_h(N_0) \in N_h, \ \Phi_h^0 = I_h(\Phi_0) \in N_h$$  \hspace{1cm} (5.4)

where we consider for simplicity that $T_0$, $N_0$, $\Phi_0 \in C^0(\Omega)$.

Finally, the functions $\hat{f}_i$ for $i = 1, 2, 3$ which appear in (5.1), (5.2) and (5.3), have the following definitions:

$$\begin{align*}
\hat{f}_1\left(T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k\right) &= \rho P\left(\Phi_h^k, T_h^k\right) \left( T_h^k \left(1 - \frac{T_h^{k+1}}{K}\right) - T_h^{k+1} \left(\frac{N_h^k + \Phi_h^k}{K}\right)\right) - \\
&- \alpha T_h^{k+1} \sqrt{1 - P\left(\Phi_h^k, T_h^k\right)^2} - \beta_1 N_h^k T_h^{k+1},
\end{align*}$$  \hspace{1cm} (5.5)

$$\begin{align*}
\hat{f}_2\left(T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k, \Phi_h^{k+1}\right) &= \alpha T_h^{k+1} \sqrt{1 - P\left(\Phi_h^k, T_h^k\right)^2} + \beta_1 N_h^k T_h^{k+1} + \delta T_h^{k+1} \Phi_h^{k+1} + \\
&+ \beta_2 N_h^k \Phi_h^{k+1},
\end{align*}$$  \hspace{1cm} (5.6)

$$\begin{align*}
\hat{f}_3\left(T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k, \Phi_h^{k+1}\right) &= \gamma \frac{T_h^{k+1}}{K} \sqrt{1 - P\left(\Phi_h^k, T_h^k\right)^2} \left[ \Phi_h^k \left(1 - \frac{\Phi_h^{k+1}}{K}\right)\right] - \\
&- \Phi_h^{k+1} \left(\frac{T_h^k + N_h^k}{K}\right) - \delta T_h^{k+1} \Phi_h^{k+1} - \beta_2 N_h^k \Phi_h^{k+1}.
\end{align*}$$  \hspace{1cm} (5.7)

The discretization of (5.5)-(5.7) is based in two main ideas:

1. We take an approximation of the negative reaction terms in a linear semi-implicit form and an explicit approximation of the positive reaction terms.

2. The sum of non-logistic reaction terms of (5.5)-(5.7) cancels, as in the continuous case.

**Remark 5.1.** Observe that (5.2) and (5.3) can be rewritten in a variational sense as follows:

$$\begin{align*}
\left(\delta_t N_h^{k+1}, v_2\right)_h &= \left(\hat{f}_2\left(T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k, \Phi_h^{k+1}\right), v_2\right)_h \\
\left(\delta_t \Phi_h^{k+1}, v_3\right)_h &= \left(\hat{f}_3\left(T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k, \Phi_h^{k+1}\right), v_3\right)_h
\end{align*}$$  \hspace{1cm} (5.8)\hspace{1cm} (5.9)

$\forall v \in N_h$ for $i = 2, 3$.

### 5.1 A priori energy estimates

In this part, we are going to get a priori energy estimates for the fully discrete solution $T_h^{k+1}$, $N_h^{k+1}$ and $\Phi_h^{k+1}$ of (5.1), (5.2) and (5.3) which are independent of $(h, k)$. The following two lemmas are based on the hypothesis of acute triangulations to get a discrete maximum principle, see [5].

**Lemma 5.1** (Lower bounds; positivity). Let $T_h^k$, $N_h^k$, $\Phi_h^k \in N_h$ such that $0 \leq T_h^k$, $N_h^k$, $\Phi_h^k$ in $\Omega$. Then, $T_h^{k+1}$, $N_h^{k+1}$, $\Phi_h^{k+1}$ $\geq 0$ in $\Omega$.

**Proof.** Let $I_h((T_h^{k+1})_-) \in N_h$ be defined as

$$I_h\left((T_h^{k+1})_-\right) = \sum_{a \in N_h} (T_h^{k+1}(a))_- \varphi_a,$$

$$\forall a \in N_h$$
where \( (T_h^{k+1}(a))_- = \min \{0, T_h^{k+1}(a)\} \). Analogously, one defines \( I_h((T_h^{k+1})_+) \in \mathbb{N}_h \) as

\[
I_h \left( (T_h^{k+1})_+ \right) = \sum_{a \in \mathbb{N}_h} (T_h^{k+1}(a))_+ \varphi_a,
\]

where \( (T_h^{k+1}(a))_+ = \max \{0, T_h^{k+1}(a)\} \). Notice that \( T_h^{k+1} = I_h((T_h^{k+1})_-) + I_h((T_h^{k+1})_+) \).

On choosing \( v = I_h((T_h^{k+1})_-) \) in (5.1), it follows that

\[
\frac{1}{dt} \left\| (T_h^{k+1})_- \right\|^2_\mathbb{R} + \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla T_h^{k+1}, \nabla I_h \left( (T_h^{k+1})_- \right) \leq \left( \hat{f}_1 \left( T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k \right), \left( T_h^{k+1} \right)_- \right)_h,
\]

where we have used in the left hand side that in every node \( a \in \mathbb{N}_h \),

\[
\delta_t T_h^{k+1}(a) \cdot (T_h^{k+1}(a))_- = \frac{1}{dt} \left( \left( T_h^{k+1}(a) \right)_- \right)^2 \geq \frac{1}{dt} \left( \left( T_h^{k+1}(a) \right)_- \right)^2
\]

using that \( T_h^k(a) \geq 0 \) and \( (T_h^{k+1}(a))_- \leq 0 \). Now, we can make the following

\[
\left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla T_h^{k+1}, \nabla I_h \left( (T_h^{k+1})_- \right) =
\]

\[
= \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla I_h \left( (T_h^{k+1})_- \right), \nabla I_h \left( (T_h^{k+1})_- \right) +
\]

\[
+ \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla I_h \left( (T_h^{k+1})_+ \right), \nabla I_h \left( (T_h^{k+1})_- \right) =
\]

\[
= \left\| \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla I_h \left( (T_h^{k+1})_- \right) \right\|^2_{L^2(\Omega)} +
\]

\[
+ \sum_{a \neq \tilde{a} \in \mathbb{N}_h} \left( T_h^{k+1}(a) - (T_h^{k+1}(\tilde{a}))_- \right) \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla \varphi_a, \nabla \varphi_{\tilde{a}}.
\]

Hence, using that \( (T_h^{k+1}(a))_-(T_h^{k+1}(\tilde{a}))_+ \leq 0 \) if \( a \neq \tilde{a} \), \( (\kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0) \) is a nonnegative function and that

\[
\nabla \varphi_a \cdot \nabla \varphi_{\tilde{a}} \leq 0 \quad \forall a \neq \tilde{a} \in \mathbb{N}_h
\]

(owing to an acute triangulation is assumed), we deduce,

\[
\left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla T_h^{k+1}, \nabla I_h \left( (T_h^{k+1})_- \right) \geq
\]

\[
\geq \left\| \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla I_h \left( (T_h^{k+1})_- \right) \right\|^2_{L^2(\Omega)}.
\]

Adding (5.11) in (5.10), it holds that

\[
\frac{1}{dt} \left\| (T_h^{k+1})_- \right\|^2_\mathbb{R} + \left\| \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla I_h \left( (T_h^{k+1})_- \right) \right\|^2_{L^2(\Omega)} \leq
\]

\[
\leq \left( \hat{f}_1 \left( T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k \right), \left( T_h^{k+1} \right)_- \right)_h \leq 0.
\]
For the last inequality above, we used that in every node \( a \in \mathcal{N}_h \) we have, due to the form of \( \hat{f}_1 \) given in (5.5), the following
\[
\rho \, P \left( \Phi^k_h(a), T^k_h(a) \right) \left( T^{k+1}_h(a) \right)_- \leq 0
\]
and
\[
- \left( \rho \, P \left( \Phi^k_h(a), T^k_h(a) \right) \left( \frac{T^k_h(a) + N^k_h(a) + \Phi^k_h(a)}{K} \right) + \alpha \sqrt{1 - P \left( \Phi^k_h(a), T^k_h(a) \right)^2} \right)
+ \beta_1 \, N^k_h(a) \left( T^{k+1}_h(a) \right)_- \leq 0.
\]
Therefore, from (5.12), \( T^{k+1}_h(a)_- \equiv 0 \) and this implies \( T^{k+1}_h \geq 0 \) in \( \Omega \).

For (5.3), the same argument can be used and it is even easier. Thus, multiplying (5.3) by \( (\Phi^{k+1}_h(a))_- \),
\[
\frac{1}{dt} \left( \Phi^{k+1}_h(a) \right)_- \leq \hat{f}_3 \left( T^k_h(a), T^{k+1}_h(a), N^k_h(a), \Phi^k_h(a), \Phi^{k+1}_h(a) \right) \left( \Phi^{k+1}_h(a) \right)_- \leq 0 \quad (5.13)
\]
since in every node \( a \in \mathcal{N}_h \) we have, due to the form of \( \hat{f}_3 \) given in (5.7), the following
\[
\gamma \, \frac{T^{k+1}_h(a)}{K} \sqrt{1 - P \left( \Phi^k_h(a), T^k_h(a) \right)^2} \left( \Phi^k_h(a) \right) \left( \Phi^{k+1}_h(a) \right)_- \leq 0
\]
and
\[
- \left( \gamma \, \frac{T^{k+1}_h(a)}{K} \sqrt{1 - P \left( \Phi^k_h(a), T^k_h(a) \right)^2} \left( \frac{T^k_h(a) + N^k_h(a) + \Phi^k_h(a)}{K} \right) + \delta \, T^{k+1}_h(a) \right)
+ \beta_2 \, N^k_h(a) \left( \Phi^{k+1}_h(a) \right)_- \leq 0.
\]
Therefore, from (5.13), \( (\Phi^{k+1}_h(a))_- \equiv 0 \forall a \in \mathcal{N}_h \) and this implies \( \Phi^{k+1}_h \geq 0 \) in \( \Omega \).

Finally, for (5.2) it is easy to obtain that
\[
\frac{1}{dt} \left( N^{k+1}_h(a) \right)_- \leq \hat{f}_2 \left( T^k_h(a), T^{k+1}_h(a), N^k_h(a), \Phi^k_h(a), \Phi^{k+1}_h(a) \right) \left( N^{k+1}_h(a) \right)_- \leq 0
\]
since \( \hat{f}_2 \left( T^k_h(a), T^{k+1}_h(a), N^k_h(a), \Phi^k_h(a), \Phi^{k+1}_h(a) \right) \geq 0 \) in every node \( a \in \mathcal{N}_h \) due to the form of \( \hat{f}_2 \) given in (5.6). Hence, \( (N^{k+1}_h(a))_- \equiv 0 \forall a \in \mathcal{N}_h \) and this implies \( N^{k+1}_h \geq 0 \) in \( \Omega \).

\[\Box\]

**Lemma 5.2** (Upper bounds). Let \( T^k_h, N^k_h, \Phi^k_h \in \mathcal{N}_h \) such that \( 0 \leq T^k_h, \Phi^k_h \leq K \) and \( 0 \leq N^k_h \) in \( \Omega \). Then one has
a) \( T^{k+1}_h, \Phi^{k+1}_h \leq K \) in \( \Omega \).
b) \( N^k_h \leq N^{k+1}_h \) in \( \Omega \).
c) \( N^k_h \leq \tilde{C} \left( T_f \right) \) in \( \Omega \), for all \( k = 1, \ldots, K_f \), with \( \tilde{C} \) independent of \( (h,k) \).

**Proof.** a) We argue in a similar fashion of Lemma 5.1. In this case, by writing (5.1) as
\[
(\delta_t \left( T^{k+1}_h - K \right), v)_h + \left( (\kappa_1 \, P \left( \Phi^k_h, T^k_h \right) + \kappa_0) \nabla \left( T^{k+1}_h - K \right), \nabla v \right)_h = \left( \hat{f}_1 \left( T^k_h, T^{k+1}_h, N^k_h, \Phi^k_h \right), v \right)_h
\]

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and taking $v = I_h((T_h^{k+1} - K)_+)$, it follows that

$$\frac{1}{dt} \left\| \left( T_h^{k+1} - K \right)_+ \right\|_{L^2(\Omega)}^2 + \frac{1}{h} \left\| \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \nabla I_h \left( \left( T_h^{k+1} - K \right)_+ \right) \right\|_{L^2(\Omega)}^2 \leq \left( \widehat{f}_1 \left( T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k \right), \left( T_h^{k+1} - K \right)_+ \right)_h \leq 0$$

since in every node $a \in \mathcal{N}_h$ we have on one side that

$$\delta_h \left( \left( T_h^{k+1} - K \right)(a) \right) \cdot \left( \left( T_h^{k+1} - K \right)(a) \right)_+ = \left( \left( T_h^{k+1} - K \right)(a) \right)_+^2 - \left( \left( T_h^K - K \right)(a) \right) \cdot \left( \left( T_h^{k+1} - K \right)(a) \right)_+ \geq \left( \left( T_h^{k+1} - K \right)(a) \right)_+^2$$

using that $(T_h^K - K)(a) \leq 0$ and $(T_h^{k+1} - K)(a)_+ \geq 0$. On other side, in every node $a \in \mathcal{N}_h$, due to the form of $\widehat{f}_1$ given in (5.5), the following

$$\left( \rho P \left( \Phi_h^k(a), T_h^k(a) \right) T_h^k(a) \left( 1 - \frac{T_h^{k+1}(a)}{K} \right) \right) \left( \left( T_h^{k+1} - K \right)(a) \right)_+ \leq 0$$

and

$$- \left( \rho P \left( \Phi_h^k(a), T_h^k(a) \right) \left( N_h^k(a) + \Phi_h^k(a) \right) K - \alpha \sqrt{1 - P \left( \Phi_h^k(a), T_h^k(a) \right)^2 + \beta_1 N_h^k(a) \left( T_h^{k+1}(a) \right) \left( \left( T_h^{k+1} - K \right)(a) \right)_+ \leq 0.\right.$$  

Hence, $(T_h^{k+1} - K)_+ \equiv 0$ and this implies $T_h^{k+1} \leq K$ in $\Omega$.

With a similar reasoning, now for (5.3), we get

$$\frac{1}{dt} \left( \left( \Phi_h^{k+1} - K \right)(a) \right)_+^2 \leq \widehat{f}_3 \left( T_h^k(a), T_h^{k+1}(a), N_h^k(a), \Phi_h^k(a), \Phi_h^{k+1}(a) \right) \left( \Phi_h^{k+1}(a) - K \right)_+ \leq 0$$

Hence, $(\Phi_h^{k+1}(a) - K)_+ \equiv 0 \forall a \in \mathcal{N}_h$ and this implies $\Phi_h^{k+1} \leq K$ in $\Omega$.

b) Using that $T_h^k$, $T_h^{k+1}$, $\Phi_h^k$, $\Phi_h^{k+1}$, $N_h^k \geq 0$, we can estimate (5.2) as follows

$$ \frac{N_h^{k+1}(a) - N_h^k(a)}{dt} = \alpha T_h^{k+1}(a) \sqrt{1 - P \left( \Phi_h^k(a), T_h^k(a) \right)^2 + \beta_1 N_h^k(a) T_h^{k+1}(a) + \delta T_h^{k+1}(a) \Phi_h^{k+1}(a) + \beta_2 N_h^k(a) \Phi_h^{k+1}(a) \geq 0.}$$

Hence,

$$N_h^k(a) \leq N_h^{k+1}(a) \forall k = 0, \ldots, K_f - 1, \text{ in } \Omega.$$

c) Using that $0 \leq T_h^k, T_h^{k+1}, \Phi_h^k, \Phi_h^{k+1} \leq K$ in $\Omega$ and for all $k = 0, \ldots, K_f$, we can bound (5.2) in the following way

$$ \frac{N_h^{k+1}(a) - N_h^k(a)}{dt} \leq C_1 N_h^k(a) + C_2, \text{ in } \Omega. $$

Applying discrete Gronwall inequality pointwise for every $a \in \mathcal{N}_h$, it holds that $\forall k = 1, \ldots K_f$
Thus, we have deduced an exponential upper bound for \( N_h^k \), with a similar expression that in the continuous estimate obtained in Lemma 3.1, which depends on the initial data of necrosis and the final time \( T_f \) and is independent of \( dt \) and \( (h,k) \).

Moreover, some a priori energy estimates will be obtained. To get these estimates, we define the piecewise functions

\[
T_h^t = \begin{cases} 
T_h^{k+1} & \text{if } t \in (t_k, t_{k+1}], \\
T_h^0 & \text{if } t = 0,
\end{cases}
\]

and the same for \( N_h^{dt} \) and \( \Phi_h^{dt} \).

**Lemma 5.3.** Given \( T_h^k \), \( N_h^k \), \( \Phi_h^k \in N_h \) such that \( 0 \leq T_h^k \), \( \Phi_h^k \leq K \) and \( 0 \leq N_h^k \leq \bar{C} (T_f) \) in \( \Omega \) with \( \bar{C} (T_f) \) the upper finite bound defined in (5.15), then

\[
||T_h^{dt}||^2_{L^2(0,T_f;H^1(\Omega))} = dt \sum_{k=1}^{K_f} ||T_h^k||^2_{H^1(\Omega)} \leq C
\]

with \( C > 0 \) independent of \((h,dt)\).

**Proof.** Take \( v = T_h^{k+1} \) in (5.1) (using that \((a - b) a = \frac{1}{2} (a^2 - b^2 + (a - b)^2) \geq \frac{1}{2} (a^2 - b^2) \ \forall a, b \in \mathbb{R}) \) and estimating the right hand side, it holds that

\[
\frac{1}{2} \frac{1}{dt} \left( ||T_h^{k+1}||^2_{h} - ||T_h^k||^2_{h} \right) + \int_\Omega \left( \kappa_1 P \left( \Phi_h^k, T_h^k \right) + \kappa_0 \right) \left| \nabla T_h^{k+1} \right|^2 \leq \rho \left( T_h^k, T_h^{k+1} \right) \leq \rho K^2 \ | \Omega | .
\]

Applying Hölder and Young’s inequalities for the last right term in every node \( a \in \mathcal{N}_h \), and adding in all the time steps, we get the following energy estimate

\[
\kappa_0 dt \sum_{k=0}^{K_f-1} ||\nabla T_h^{k+1}||_{L^2(\Omega)} \leq \frac{1}{2} ||T_h^0||^2_{h} + T_f \rho K^2 \ | \Omega | .
\]

hence the desired bound is deduced.

Before presenting the energy estimate for \( N_h^{dt} \) and \( \Phi_h^{dt} \) in \( L^\infty (0, T_f; H^1(\Omega)) \) we define the Laplacian in a discrete way using the discrete \( L^2 \) product, that is \(-\Delta_h n_h \in N_h \) such that \((-\Delta_h n_h, \pi_h)_h = (\nabla n_h, \nabla \pi_h), \forall \pi_h \in N_h \). Now, we show a result of discrete Laplacian which we will use later.

**Lemma 5.4.** Given \(-\Delta_h n_h \in N_h \), it holds that

\[
|| - \Delta_h n_h ||_{L^2(\Omega)} \leq C \frac{1}{h} ||n_h||_{H^1(\Omega)} \ \forall n_h \in N_h.
\]

**Proof.** Choosing \(-\Delta_h n_h \in N_h \) as test function in the definition of discrete Laplacian, we obtain that

\[
|| - \Delta_h n_h ||^2_{h} = ( - \Delta_h n_h, - \Delta_h n_h )_h = (\nabla n_h, \nabla (- \Delta_h n_h)) \leq ||\nabla n_h||_{L^2(\Omega)} \frac{1}{h} || - \Delta_h n_h ||_{L^2(\Omega)}
\]

where we have used the inverse inequality \( ||\pi_h||_{H^1(\Omega)} \leq C \frac{1}{h} ||\pi_h||_{L^2(\Omega)} \ \forall \pi \in N_h \). On other hand, we have that \( || \cdot ||_h \) and \( || \cdot ||_{L^2(\Omega)} \) are equivalent norms, hence \( || - \Delta_h n_h ||^2_{h} \geq C || - \Delta_h n_h ||^2_{L^2(\Omega)} \).
Finally, we deduce
\[ \| - \Delta_h n_h \|_{L^2(\Omega)} \leq C \frac{1}{h} \| \nabla n_h \|_{L^2(\Omega)}. \]

**Lemma 5.5.** Given \( T_h^k, N_h^k, \Phi_h^k \in N_h \) such that \( 0 \leq T_h^k, \Phi_h^k \leq K \) and \( 0 \leq N_h^k \leq \bar{C} (T_f) \) in \( \Omega \) with \( \bar{C} (T_f) \) the upper finite bound defined in (5.15), then for small enough \( dt \), one has
\[ \left\| N_h^{d t}, \Phi_h^{d t} \right\|_{L^\infty(0,T_f; H^1(\Omega))} \leq C \]
with \( C > 0 \), independent of \((h, dt)\).

**Proof.** We make the proof for \( N_h^{d t} \) since for \( \Phi_h^{d t} \) is similar. By multiplying by \(-\Delta_h N_h^{k+1} \) in (5.8), it holds that
\[ \frac{1}{2} \frac{d}{d t} \left( \| \nabla N_h^{k+1} \|_h^2 - \| \nabla N_h^k \|_h^2 \right) \leq \left( \hat{f}_2 \left( T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k, \Phi_h^{k+1} \right), -\Delta_h N_h^{k+1} \right)_h. \]
(5.16)

For the right-hand side, we use an extension of the Scott-Zhang interpolation operator \( Q_h \) from \( L^2(\Omega) \) to \( N_h \) (see [13, Proposition 2.4] and the references therein) in the following way
\[ \left( \hat{f}_2, -\Delta_h N_h^{k+1} \right)_h = \left( \hat{f}_2 - Q_h \hat{f}_2, -\Delta_h N_h^{k+1} \right)_h + \left( Q_h \hat{f}_2, -\Delta_h N_h^{k+1} \right)_h \]
where we denoted \( \hat{f}_2 = \hat{f}_2 \left( T_h^k, T_h^{k+1}, N_h^k, \Phi_h^k, \Phi_h^{k+1} \right) \) in order to simplify the notation.

Now, we bound (5.17) using that \( \| \hat{f}_2 - Q_h \hat{f}_2 \|_{L^2(\Omega)} \leq C h \| \hat{f}_2 \|_{H^1(\Omega)}, \| Q_h \hat{f}_2 \|_{H^1(\Omega)} \leq C \| \hat{f}_2 \|_{H^1(\Omega)} \) and Lemma 5.5 to obtain that
\[ \left( \hat{f}_2 - Q_h \hat{f}_2, -\Delta_h N_h^{k+1} \right)_h + \left( Q_h \hat{f}_2, -\Delta_h N_h^{k+1} \right)_h \leq \left( \hat{f}_2 - Q_h \hat{f}_2, -\Delta_h N_h^{k+1} \right)_h + \left( \nabla Q_h \hat{f}_2, \nabla N_h^{k+1} \right) \leq C h \| \hat{f}_2 \|_{H^1(\Omega)} \| \nabla N_h^{k+1} \|_{L^2(\Omega)} + C \| \hat{f}_2 \|_{H^1(\Omega)} \| \nabla N_h^{k+1} \|_{L^2(\Omega)} \leq C \| \hat{f}_2 \|_{H^1(\Omega)} \| \nabla N_h^{k+1} \|_{L^2(\Omega)} \].

In these circumstances, we can follow a similar argument to (3.20) in an discrete way
\[ C \| \hat{f}_2 \|_{H^1(\Omega)} \| \nabla N_h^{k+1} \|_{L^2(\Omega)} \leq C \left( 1 + \| \nabla T_h^k, \nabla T_h^{k+1}, \nabla N_h^k, \nabla \Phi_h^k, \nabla \Phi_h^{k+1} \|_{L^2(\Omega)} \right) \| \nabla N_h^{k+1} \|_{L^2(\Omega)} \leq C \left( 1 + \| \nabla T_h^k, \nabla T_h^{k+1}, \nabla N_h^k, \nabla N_h^{k+1}, \nabla \Phi_h^k, \nabla \Phi_h^{k+1} \|_{L^2(\Omega)}^2 \right). \]

Hence,
\[ \frac{1}{2} \frac{d}{d t} \left( \| \nabla N_h^{k+1} \|_h^2 - \| \nabla N_h^k \|_h^2 \right) \leq C \left( 1 + \| \nabla T_h^k, \nabla T_h^{k+1}, \nabla N_h^k, \nabla N_h^{k+1}, \nabla \Phi_h^k, \nabla \Phi_h^{k+1} \|_{L^2(\Omega)}^2 \right). \]
(5.18)

We can obtain a similar expression for \( \Phi_h^{d t} \)
\[ \frac{1}{2} \frac{d}{d t} \left( \| \nabla \Phi_h^{k+1} \|_h^2 - \| \nabla \Phi_h^k \|_h^2 \right) \leq C \left( 1 + \| \nabla T_h^k, \nabla T_h^{k+1}, \nabla N_h^k, \nabla \Phi_h^k, \nabla \Phi_h^{k+1} \|_{L^2(\Omega)}^2 \right). \]
(5.19)
Adding \((5.18)\) and \((5.19)\), multiplying by 2 \(dt\) and adding with respect \(k = 0, \ldots, \tilde{k} - 1\) with \(0 \leq \tilde{k} \leq K_f\), we have (using that \(\|\cdot\|_h\) is an equivalent norm to \(L^2\))

\[
\left\| \nabla N_{\tilde{k}}^h, \nabla \Phi_{\tilde{k}}^h \right\|_{L^2(\Omega)}^2 \leq C \left( T_f + dt \sum_{k=0}^{\tilde{k}} \left\| \nabla T_k^h, \nabla N_k^h, \nabla \Phi_k^h \right\|_{L^2(\Omega)}^2 \right) + C \left\| \nabla N_0^h, \nabla \Phi_0^h \right\|_{L^2(\Omega)}^2. \tag{5.20}
\]

We can apply discrete Gronwall Lemma for any \(dt\) small enough such that \(C \ dt \leq \delta_0 < 1\), to obtain

\[
\left\| \nabla N_{\tilde{k}}^h, \nabla \Phi_{\tilde{k}}^h \right\|_{L^2(\Omega)}^2 \leq \frac{C}{1 - \delta_0} \left( T_f + dt \sum_{k=0}^{K_f} \left\| \nabla T_k^h \right\|_{L^2(\Omega)}^2 + C \left\| \nabla N_0^h, \nabla \Phi_0^h \right\|_{L^2(\Omega)}^2 \right) e^{\frac{C}{1 - \delta_0} T_f}. \]

Since \(\nabla T_k^h\) is bounded in \(L^2(0, T_f; L^2(\Omega))\), we deduce,

\[
\left( \nabla N_k^h, \nabla \Phi_k^h \right) \text{ is bounded in } L^\infty (0, T_f; L^2(\Omega)).
\]

Hence,

\[
\left( N_k^h, \Phi_k^h \right) \text{ is bounded in } L^\infty (0, T_f; H^1(\Omega)).
\]

\[\square\]

5.2 Numerical Simulations

The main goals of this section consist of:

1. Validate numerically the properties of the scheme \((5.1)-(5.3)\), namely, the pointwise and energy estimates.

2. Compare \((5.1)-(5.3)\) with two simplifications schemes: The first one changing the time approximation for a completely explicit scheme and later changing the space approximation for the scheme \((5.1)-(5.3)\) without "mass-lumping".

We start computing the lower and upper bounds of \(T_{k+1}^h\) for these schemes. We consider \(T_f = 1\), time step \(dt = 10^{-2}\), mesh size \(h = 0.025\) and the parameters are taken as:

| Parameter | \(\kappa_1\) | \(\kappa_0\) | \(\rho\) | \(\alpha\) | \(\beta_1\) | \(\beta_2\) | \(\gamma\) | \(\delta\) | \(K\) |
|-----------|-------------|-------------|---------|---------|---------|---------|---------|---------|------|
| Value     | \(8 \cdot 10^{-5}\) | \(8 \cdot 10^{-5}\) | 1       | 0.8     | 0.8     | 0.8     | 0.008   | 0.8     | 1    |

Table 2: Parameters value.

We take the initial vasculature \(\Phi_0(x) = 0.5\) and the initial conditions for the tumor and necrosis given in Figure 1

(a) Initial tumor. (b) Initial necrosis.

Figure 1: Initial tumor and necrosis.
We show in Figure 2 the minimum and maximum value of $T_h^{k+1}$ in the first 10 time steps using IMEX and completely explicit scheme:

![Figure 2: Pointwise estimate for $T_h^{k+1}$ versus time using IMEX and completely explicit scheme.](image)

We observe that lower and upper bounds are not satisfied for the completely explicit scheme while for IMEX scheme we get the pointwise estimates proved in Lemmas 5.1 and 5.2. Moreover, taking the mesh size $h$ smaller, the completely explicit scheme has a similar behaviour. Hence, we can conclude that the explicit time approximation does not satisfy the maximum principle.

In our second numerical simulation, we compare graphically the lower bound of $T_h^{k+1}$ for our scheme (5.1)-(5.3) and for the same scheme (5.1)-(5.3) but without "mass-lumping". We consider $T_f = 1$, time step $dt = 10^{-2}$, $h = 0.1$ and the parameters are taken as:

| Parameter | $\kappa_1$ | $\kappa_0$ | $\rho$ | $\alpha$ | $\beta_1$ | $\beta_2$ | $\gamma$ | $\delta$ | $K$ |
|-----------|-------------|-------------|--------|----------|-----------|-----------|----------|--------|-----|
| Value     | $8 \cdot 10^{-4}$ | $8 \cdot 10^{-4}$ | 1      | 0        | 0         | 0         | 0        | 0      | 1   |

Table 3: Parameters value.

We take again the initial vasculature $\Phi_0(x) = 0.5$ and the initial conditions for the tumor and necrosis given in Figure 1. We show in Figure 3 the minimum value of $T_h^{k+1}$ in 40 time step using IMEX with "mass-lumping" and IMEX without "mass-lumping":

![Figure 3: Minimum value of $T_h^{k+1}$ using IMEX with "mass-lumping" and IMEX without "mass-lumping".](image)

We observe how positivity is not satisfied for IMEX without "mass-lumping" while it is conserved.
for IMEX with "mass-lumping", in agreement with Lemma 5.1. Moreover, taking the time step $dt$ smaller, we do not get positivity for scheme (5.1)-(5.3) without "mass-lumping". Hence, we can conclude that the space approximation without "mass-lumping" does not satisfy positivity.

Thus, we have proved that the completely explicit scheme and the IMEX without "mass-lumping" do not satisfy positivity.

Finally, we are going to check the energy estimate of $T_{k+1}^{h}$ obtained in Lemma 5.3 for our scheme (5.1)-(5.3) and for a completely explicit scheme and finite element with "mass-lumping". Now, we consider $T_f = 0.01$, the mesh size $h = 0.025$, the same initial condition than in Figure (1) and the parameters are taken as:

| Parameter | $\kappa_1$ | $\kappa_0$ | $\rho$ | $\alpha$ | $\beta_1$ | $\beta_2$ | $\gamma$ | $\delta$ | $K$ |
|-----------|------------|------------|--------|---------|-----------|----------|--------|--------|-----|
| Value     | $2.9 \cdot 10^{-7}$ | $2.9 \cdot 10^{-7}$ | 1      | 0.0029  | 0.0029    | 0        | 0.0029 | 0.0029 | 1   |

Table 4: Parameters value.

We show in Figure 4 the value of $\|T_{k}^{dt}\|_{L^2(0,T_f;H^1(\Omega))}^2$ for the different $dt$ obtained with $K_f = 10, 60, 110, 160, 210, 260, 310, 360, 410, 460, 510$. using the IMEX and completely explicit scheme.

![Figure 4: Value of $\|T_{k}^{dt}\|_{L^2(0,T_f;H^1(\Omega))}^2$ versus time using IMEX and completely explicit scheme.](image)

We observe that the difference between the value of $\|T_{k}^{dt}\|_{L^2(0,T_f;H^1(\Omega))}^2$ using these two schemes increases as $dt$ increases.

**Remark 5.2.** We have presented some numerical simulations in order to verify the analytical results of Section 5. In a forthcoming paper, [12], we will explore the behaviour of the model depending on the parameter using appropriate numerical simulations. In particular, we will study different situations such as tumor growth with vasculature non-uniformly distributed. Moreover, in all the above simulations, the hypothesis (4.6) is satisfied and hence tumor, $T$, and vasculature, $\Phi$, will vanish at infinity time. When the proliferating part of the tumor, $T$, goes to zero, only the necrotic part, $N$, remains. This situation represents that the tumor remains encapsulated, it could not longer grow.

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