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Theoretical and numerical results of the quorum sensing model in a bacterial biofilm coupled with the heat equation

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Abstract. In this work, we propose a non-linear reaction-diffusion model coupled with the heat equation, modeling the action of antibiotics as well as quorum-sensing inhibitors on the virulence of bacterial biofilms in the presence of temperature effects. We prove the well-posedness of the system using semigroup theory. Then, we approximate the system by a standard finite element scheme in space and an implicit Euler method in time. Finally, numerical simulations using MATLAB are presented to validate the obtained results.

1 Introduction

Biofilms are bacterial clumps that stick to wet surfaces, a self-produced polymeric matrix [11], and they are essentially described as a community of microorganisms (bacteria, fungi, algae, and protozoa) attached to surfaces. Biofilms are a phenomenon that we encounter in our daily lives. There are two types of biofilms: beneficial biofilms, such as biological barriers that protect soil from contamination and water purification systems, among others, and harmful biofilms that cause many problems, such as hospital-acquired infections. The bacteria Pseudomonas aeruginosa and Staphylococcus aureus are among the most prominent human pathogens.

We are interested in medical fields, where bacterial growth and virulence depend on nutrient availability and their ability to communicate with each other using chemical signaling molecules[18]. This mechanism, known as quorum-sensing (QS), allows bacteria to activate certain genes only when a specific chemical signal reaches a specific concentration. Several studies have focused on the complex quorum-sensing system in Pseudomonas aeruginosa, where signaling molecules called N-Acylated Homoserine Lactones (AHLs), such as 3-oxo-C12-HSL, bind to gene-regulatory protein LasR to activate the expression of target genes. In the early stages of infection, when bacterial density is low, they remain relatively unnoticed by the immune system. However, when bacterial populations increase, they use the QS mechanism to rapidly and synchronously activate virulence genes, leading to the production of virulence factors that can overwhelm the body's defenses. Bacteria such as Pseudomonas aeruginosa and Staphylococcus aureus are increasingly resistant to antibiotics.

In [28], Williams proposed the idea of targeting the quorum-sensing system to treat bacterial infections by disrupting bacterial-cell communication to prevent the activation of virulence genes. In some studies, mathematical models have been built that simulate the effect of enzymes that degrade AHLs or drugs that degrade LasR, along with the use of antibiotics, to reduce the virulence of these bacteria.

In [6], Blouza proposes a system of partial differential equations (PDEs) in a two-dimensional environment to study the effect of quorum-sensing in Pseudomonas aeruginosa when combined with antibiotics and presents numerical results. We are interested in this model and will review below how he developed it.

The proposed model is formulated as a coupled system of nonlinear reaction-diffusion equations [20], defined on $\Omega \times [0,T]$ with $T > 0$, where $\Omega \subset \mathbb{R}^2$ is a bounded domain whose boundary is decomposed as $\partial\Omega = \Gamma_N \cup \Gamma_D$, with $\Gamma_N \cap \Gamma_D = \emptyset$. The substrate S is injected through a part of its boundary Γ_D. The nutrient diffuses into and out of the bacterial cells at the same rate and is consumed by the total biomass $\psi + \varphi$ following Monod kinetics. Hence, the evolution of the nutrient is described as:

$$\frac{\partial S}{\partial t} = d_S \Delta S - k_1 \frac{S}{k_2 + S} (\psi + \varphi),$$

where S is the concentration of the nutrient, ψ the concentration of the down-regulated cells, φ the concentration of the up-regulated cells, k_1 the maximum consumption rate, k_2 the Monod half-saturation constant, and d_S the nutrient diffusion coefficient.

From the mass-balance principle, the evolution of the total biomass M is modeled by:

$$\frac{\partial M}{\partial t} = \nabla (D(M) \nabla M) + G(u, M),$$

where $G(u, M)$ expresses the growth of the biomass and $D(M) \approx P'(M)$ with P the unknown biofilm pressure. Then, we assume that $D(M)$ does not depend on M. This assumption is not too restrictive since we are not concerned with the biofilm shape.

The up-regulated cells are converted to down-regulated cells at a constant rate. Hence, it holds that:

$$\begin{array}{l} \frac{\partial \psi}{\partial t} = d\Delta\psi + k_3 \frac{S}{k_3+S}\psi - k_5 A^m \psi + k_5 \varphi - k_4 \psi \\ \frac{\partial \varphi}{\partial t} = d\Delta\varphi + k_3 \frac{S}{k_3+S}\varphi + k_5 A^m \psi - k_5 \psi - k_4 \varphi \end{array},$$

where k_3 is the maximum growth rate, k_4 the lysis rate, k_5 the quorum-sensing regulation rate, and v the antibiotic concentration.

Thus, the biofilm is defined by the domain:

$$\{x \in \Omega; \psi(x,t) + \varphi(x,t) > 0\}.$$

The AHL molecules diffuse through the domain. The AHL molecules decay abiotically at rate γ. Down-regulated cells produce the signaling molecule at rate, whereas up-regulated cells produce it at the increased rate $\alpha+\beta$, where is one order of magnitude larger than. The signaling molecule production rate of the up-regulated cells is higher than the abiotic decay rate, where $\alpha + \beta > \gamma$,

$$\frac{\partial A}{\partial t} = d_2 \Delta A - \gamma A + \alpha \frac{RA}{K_L + RA}\psi + (\alpha + \beta) \frac{RA}{K_L + RA}\varphi.$$

The LasR protein is involved in the production of the LasR/3-oxo-C12-HSL (whose concentration is proportional to RA, [2]), degrades naturally at a constant rate k_R, and is blocked by the QSB agent. Hence, we get:

$$\frac{\partial R}{\partial t} = d_R \Delta R - k_R R + k_3 \frac{RA}{k_R + RA} - k_3 \frac{X+Y}{k_2 + X + Y} R + k_R R Q,$$

the antibiotic diffuses in the culture at rate d_u, degrades at rate l_u, and reacts with the down-regulated cell at rate k_u. Thus, we obtain:

$$\frac{\partial u}{\partial t} = d_v \Delta v - l_v v - k_v \psi v.$$

Finally, we assume that the QSB agent diffuses in the culture at rate d_Q, degrades at rate l_Q, and reacts with the down-regulated cell at rate k_Q:

$$\frac{\partial q}{\partial t} = d_Q \Delta Q - l_Q Q - k_v R Q.$$

Then the system is given by:

$$\begin{cases} \frac{\partial S}{\partial t} = d_s \Delta s - k_1 \frac{S}{k_2+S} (\psi + \varphi) \\ \frac{\partial A}{\partial t} = d_2 \Delta A - \gamma A + \alpha \frac{RA}{K_L+RA} \psi + (\alpha+\beta) \frac{RA}{K_L+RA} \varphi \\ \frac{\partial \psi}{\partial t} = d \Delta \psi + k_3 \frac{S}{k_3+S} \psi - k_5 A^m \psi + k_5 \varphi - k_4 \psi \\ \frac{\partial \varphi}{\partial t} = d \Delta \varphi + k_3 \frac{S}{k_3+S} \varphi + k_5 A^m \psi - k_5 \psi - k_4 \varphi \\ \frac{\partial R}{\partial t} = d_R \Delta R - k_R R + k_3 \frac{RA}{k_R+RA} - k_3 \frac{X+Y}{k_2+X+Y} R \end{cases} . \tag{1.1}$$

In this work, we propose a system of coupled reaction-diffusion equations incorporating quorum sensing, antibiotic response, and temperature-dependent biofilm dynamics. The model includes bacterial populations, nutrient concentration, signal molecules, and temperature evolution governed by a heat equation, where temperature affects bacterial growth, quorum sensing, and biofilm development. The heat generated by bacterial metabolism provides feedback into the temperature field. This has important applications such as simulating the behavior of bacteria in environments with variable temperatures (such as infection sites, medical implants, or industrial systems), and studying the effects of temperature modification (such as heat treatment) or cooling strategies on bacterial biofilms.

The heat equation describes the evolution of temperature in space and time. It takes the form:

$$\frac{\partial T}{\partial t} = k \Delta T + q,$$

where $T(x,t)$ is the temperature at spatial location x and time t, k is the thermal diffusivity, and q is the source term representing heat production or loss, such as due to the metabolic activity of bacteria or external sources. In the case of modeling quorum sensing in a bacterial biofilm in the presence of temperature, the temperature affects different components of the system, such as the rates of reaction, diffusion, or growth. At the same time, the metabolic activities of bacteria can affect q in the heat equation, creating a two-way correlation.

The temperature-dependent parameters are the reaction rates $(k_1, k_3, k_4, k_5, \alpha, \beta, \gamma)$, following an Arrhenius-like relationship:

$$\tilde{k}(T) = k_0 e^{-\frac{E_a}{pT}},$$

where, k_0 Pre-exponential factor (rate at a reference temperature), E_a Activation energy,

p Gas constant. For example, bacterial growth and quorum-sensing production rates can be enhanced or suppressed depending on T.

Heat Source q: Bacterial metabolism can act as a heat source, proportional to bacterial concentration (ψ, φ) or their metabolic activity

$$q = q_0(\psi + \varphi),$$

where q_0 is a proportionality constant linking bacterial concentration to heat production. Then the coupled system is given by:

$$\begin{cases} \frac{\partial S}{\partial t} = d_s \Delta s - k_1 (T) \frac{S}{k_2+S} (\psi + \varphi) \\ \frac{\partial A}{\partial t} = d_2 \Delta A - \gamma (T) A + \alpha (T) \frac{RA}{K_L+RA} \psi + (\alpha (T) + \beta (T)) \frac{RA}{K_L+RA} \varphi \\ \frac{\partial \psi}{\partial t} = d \Delta \psi + k_3 (T) \frac{S}{k_3+S} \psi - k_5 (T) A^m \psi + k_5 (T) \varphi - k_4 (T) \psi \\ \frac{\partial \varphi}{\partial t} = d \Delta \varphi + k_3 (T) \frac{S}{k_3+S} \varphi + k_5 (T) A^m \psi - k_5 (T) \psi - k_4 (T) \varphi \\ \frac{\partial R}{\partial t} = d_R \Delta R - k_R (T) R + k_3 (T) \frac{RA}{k_R+RA} - k_3 (T) \frac{\psi+\varphi}{k_2+\psi+\varphi} R \\ \frac{\partial T}{\partial t} = k \Delta T + q_0(\psi + \varphi) \end{cases} , \tag{1.2}$$

we complete the system with the boundary and initial conditions given below:

$$\begin{aligned} \nabla S(x,t).n &= \nabla \psi(x,t).n = \nabla \varphi(x,t).n = 0, (x,t) \in \partial\Omega \times (0,T), \qquad (1.3) \\ \nabla A(x,t).n &= \nabla R(x,t).n = \nabla T(x,t).n = 0, (x,t) \in \partial\Omega \times (0,T), \\ S(x,0) &= S_0,\ \psi(x,0) = \psi_0,\ \varphi(x,0) = \varphi_0,\ A(x,0) = A_0, \\ R(x,0) &= R_0,\ T(x,0) = T_0, x \in \Omega. \end{aligned}$$

The main contributions of this work are: We introduce a novel QS-heat model for bacterial biofilms, including temperature-dependent reaction rates and metabolic heat production. We prove the existence and uniqueness of solutions using semigroup theory. We propose a finite element-Euler time discretization scheme and analyze its stability. We implement the numerical method in MATLAB and present simulations showing the influence of temperature on biofilm dynamics. The structure of this manuscript is as follows. In Section 1, we introduce the model and state our assumptions. Section 2 establishes well-posedness of the coupled PDE system using semigroup theory. In Section 3, we present a numerical scheme based on finite elements in space and the backward Euler method in time, and provide error estimates [21]. Section 4 shows numerical simulations in MATLAB that demonstrate how temperature variation affects quorum sensing and biofilm formation.

2 Preliminaries

In this study, we make use of the following assumptions:

(H_1) The functions $S(x,t)$, $A(x,t)$, $\psi(x,t)$, $\varphi(x,t)$, $R(x,t)$, and $T(x,t)$ are bounded; that is, there exists a constant $M > 0$ such that

$$|S(x,t)|,\ |A(x,t)|,\ |\psi(x,t)|,\ |\varphi(x,t)|,\ |R(x,t)|,\ |T(x,t)| < M.$$

(H_2) The functions $k_1(T)$, $k_2(T)$, $k_3(T)$, $k_4(T)$, $k_5(T)$, $\alpha(T)$, $\beta(T)$, and $\gamma(T)$ are continuously differentiable, and hence Lipschitz continuous on bounded intervals.

3 The well-posedness of the problem

In this section, we prove the existence and uniqueness for problem (1.2), we denote the vector function $\Phi = (S, A, \psi, \varphi, R, T)^\top$. Then, the system (1.2) can be written as:

$$\begin{cases} \Phi_t = A\Phi + F(\Phi) \ ; \ t > 0 \\ \Phi(0) = \Phi_0 = (S_0, A_0, \psi_0, \varphi_0, R_0, T_0)^\top \end{cases}, \tag{3.1}$$

where

$$A\Phi = \begin{pmatrix} d_S \Delta S \\ d_2 \Delta A \\ d\Delta\psi \\ d\Delta\varphi \\ d_R \Delta R \\ k\Delta T \end{pmatrix},$$

and

$$F(\Phi) = \begin{pmatrix} F_1(\Phi) \\ F_2(\Phi) \\ F_3(\Phi) \\ F_4(\Phi) \\ F_5(\Phi) \\ F_6(\Phi) \end{pmatrix} = \begin{pmatrix} -k_1(T)\frac{S}{k_2+S}(\psi+\varphi) \\ -\gamma(T)A + \alpha(T)\frac{RA}{K_L+RA}\psi + (\alpha(T)+\beta(T))\frac{RA}{K_L+RA}\varphi \\ k_3(T)\frac{S}{k_3+S}\psi - k_5(T)A^m\psi + k_5(T)\varphi - k_4(T)\psi \\ k_3(T)\frac{S}{k_3+S}\varphi + k_5(T)A^m\psi - k_5(T)\psi - k_4(T)\varphi \\ -k_R(T)R + k_3(T)\frac{RA}{k_R+RA} - k_3(T)\frac{\psi+\varphi}{k_2+\psi+\varphi}R \\ q_0(\psi+\varphi) \end{pmatrix},$$

so the linear operator $A : D(A) \subset H \to H$ is defined by:

$$A = \begin{pmatrix} d_S\Delta & 0 & 0 & 0 & 0 & 0 \\ 0 & d_2\Delta & 0 & 0 & 0 & 0 \\ 0 & 0 & d\Delta & 0 & 0 & 0 \\ 0 & 0 & 0 & d\Delta & 0 & 0 \\ 0 & 0 & 0 & 0 & d_R\Delta & 0 \\ 0 & 0 & 0 & 0 & 0 & k\Delta \end{pmatrix},$$

where the space H is given by:

$$H = H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega),$$

such that

$$\begin{aligned} H_*^1(\Omega) &= \{w \in H^1(\Omega), \nabla w_{/\partial\Omega} = 0\} \\ L_*^2(\Omega) &= \{w \in L^2(\Omega); \nabla w_{/\partial\Omega} = 0\} \\ X &= L_*^2(\Omega) \times L_*^2(\Omega) \times L_*^2(\Omega) \times L_*^2(\Omega) \\ H_*^2(\Omega) &= \{w \in H^2(\Omega), \nabla w_{/\partial\Omega} = 0\}, \end{aligned}$$

we equip H with the inner product defined by:
for any $\Phi = (S, A, \psi, \varphi, R, T)^\top \in H$ and $\Phi' = (\tilde{S}, \tilde{A}, \tilde{\psi}, \tilde{\varphi}, \tilde{R}, \tilde{T})^\top \in H$

$$\langle \Phi, \tilde{\Phi} \rangle = \int_\Omega S.\tilde{S}dx + \int_\Omega A.\tilde{A}dx + \int_\Omega \psi.\tilde{\psi}dx + \int_\Omega \varphi.\tilde{\varphi}dx + \int_\Omega R.\tilde{R}dx + \int_\Omega T.\tilde{T}dx,$$

the associated norm $\|\cdot\|_H$ is equivalent to the usual one.
The domain of A is given by:

$$D(A) = \left\{ \begin{array}{c} \Phi \in H;\ S \in H_*^1(\Omega) \cap H_*^2(\Omega),\ A \in H_*^1(\Omega) \cap H_*^2(\Omega),\ \psi \in H_*^1(\Omega) \cap H_*^2(\Omega), \\ \varphi \in H_*^1(\Omega) \cap H_*^2(\Omega),\ R \in H_*^1(\Omega) \cap H_*^2(\Omega),\ T \in H_*^1(\Omega) \cap H_*^2(\Omega) \end{array} \right\}.$$

3.1 Existence of Solutions

Clearly, $D(A)$ is dense in H.
We have:

$$\langle A\Phi, \Phi \rangle = -d_S \int_\Omega |\nabla S|^2 dx - d_2 \int_\Omega |\nabla A|^2 dx - d \int_\Omega |\nabla \psi|^2 dx - d \int_\Omega |\nabla \varphi|^2 dx$$

$$-d_R \int_\Omega |\nabla R|^2 dx - k \int_\Omega |\nabla T|^2 dx \leq 0. \tag{3.2}$$

As a result, the operator A is dissipative.
Then, we prove that the operator $(I - A)$ is surjective:
let $f = (f_1, f_2, f_3, f_4, f_5, f_6)^\top \in H$, we prove that there exists a unique $\Phi \in D(A)$ such that:

$$(I - A)\Phi = f,$$

that is:

$$\begin{cases} S - d_S \Delta S = f_1 \\ A - d_2 \Delta A = f_2 \\ \psi - d\Delta\psi = f_3 \\ \varphi - d\Delta\varphi = f_4 \\ R - d_R \Delta R = f_5 \\ T - k\Delta T = f_6 \end{cases}. \tag{3.3}$$

Now, we define over $V \times V$, where

$$V = H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega) \times H_*^1(\Omega),$$

the following bilinear form:

$$
\begin{aligned}
b\left((S,A,\psi,\varphi,R,T);(S^1,A^1,\psi^1,\varphi^1,R^1,T^1)\right) &= \int_\Omega SS^1dx + d_s\int_\Omega \nabla S\nabla S^1dx \\
&+\int_\Omega AA^1dx + d_2\int_\Omega \nabla A\nabla A^1dx \\
&+\int_\Omega \psi\psi^1dx + d\int_\Omega \nabla\psi\nabla\psi^1dx \\
&+\int_\Omega \varphi\varphi^1dx + d\int_\Omega \nabla\varphi\nabla\varphi^1dx \\
&+\int_\Omega RR^1dx + d_R\int_\Omega \nabla R\nabla R^1dx \\
&+\int_\Omega TT^1dx + k\int_\Omega \nabla T\nabla T^1dx,
\end{aligned}
$$

and the linear form:

$$
\begin{aligned}
l\left(S^1,A^1,\psi^1,\varphi^1,R^1,T^1\right) &= \int_\Omega f_1S^1dx + \int_\Omega f_2A^1dx + \int_\Omega f_3\psi^1dx \\
&+\int_\Omega f_4\varphi^1dx + \int_\Omega f_5R^1dx + \int_\Omega f_6T^1dx, \qquad (3.4)
\end{aligned}
$$

we equip V with the norm:

$$
\begin{aligned}
\|(S,A,\psi,\varphi,R,T)\|_V^2 &= \|S\|_2^2 + \|\nabla S\|_2^2 + \|A\|_2^2 + \|\nabla A\|_2^2 \\
&+ \|\psi\|_2^2 + \|\nabla\psi\|_2^2 + \|\varphi\|_2^2 + \|\nabla\varphi\|_2^2 \\
&+ \|R\|_2^2 + \|\nabla R\|_2^2 + \|T\|_2^2 + \|\nabla T\|_2^2 .
\end{aligned}
$$

By using the Cauchy-Schwarz inequality, we find:

$$
\begin{aligned}
\left|b\left((S,A,\psi,\varphi,R,T);\left(S^1,,A^1,\psi^1,\varphi^1,R^1,T^1\right)\right)\right| &\le \|S\|_2 . \left\|S^1\right\|_2 + |d_S|\,\|\nabla S\|_2 . \left\|\nabla S^1\right\|_2 \\
&+ \|A\|_2 . \left\|A^1\right\|_2 + |d_2|\,\|\nabla A\|_2 . \left\|\nabla A^1\right\|_2 \\
&+ \|\psi\|_2 . \left\|\psi^1\right\|_2 + |d|\,\|\nabla\psi\|_2 . \left\|\nabla\psi^1\right\|_2 \\
&+ \|\varphi\|_2 . \left\|\varphi^1\right\|_2 + |d|\,\|\nabla\varphi\|_2 . \left\|\nabla\varphi^1\right\|_2 \\
&+ \|R\|_2 . \left\|R^1\right\|_2 + |d_R|\,\|\nabla R\|_2 . \left\|\nabla R^1\right\|_2 \\
&+ \|T\|_2 . \left\|T^1\right\|_2 + |k|\,\|\nabla T\|_2 . \left\|\nabla T^1\right\|_2 .
\end{aligned}
$$

Let $M_1 > 0$, so

$$
\begin{aligned}
\left|b\left((S,A,\psi,\varphi,R,T);\left(S^1,A^1,\psi^1,\varphi^1,R^1,T^1\right)\right)\right| &\le M_1(\|S\|_2 + \|\nabla S\|_2 + \|\psi\|_2 + \|\nabla\psi\|_2 \\
&+ \|\varphi\|_2 + \|\nabla\varphi\|_2 + \|v\|_2 + \|\nabla v\|_2) \times \\
&(\left\|u^1\right\|_2 + \left\|\nabla u^1\right\|_2 + \left\|\psi^1\right\|_2 + \left\|\nabla\psi^1\right\|_2 \\
&+ \left\|\varphi^1\right\|_2 + \left\|\nabla\varphi^1\right\|_2 + \left\|v^1\right\|_2 + \left\|\nabla v^1\right\|_2),
\end{aligned}
$$

by estimating the above inequality, and for $M_2 > 0$, we obtain:

$$
\begin{aligned}
\left|b\left((S,A,\psi,\varphi,R,T);\left(S^1,A^1,\psi^1,\varphi^1,R^1,T^1\right)\right)\right| &\le M_2\,\|(S,A,\psi,\varphi,R,T)\|_V \\
&\left\|\left(S^1,A^1,\psi^1,\varphi^1,R^1,T^1\right)\right\|_V .
\end{aligned}
$$

And we have:

$$\begin{aligned}\left|l(S^1,A^1,\psi^1,\varphi^1,R^1,T^1)\right| &= \left|\int_\Omega f_1 S^1 dx + \int_\Omega f_2 A^1 dx + \int_\Omega f_3 \psi^1 dx \right.\\ &\left. + \int_\Omega f_4 \varphi^1 dx + \int_\Omega f_5 R^1 dx + \int_\Omega f_6 T^1 dx\right|.\end{aligned}$$

Again, by using the Cauchy-Schwarz inequality, we find:

$$\begin{aligned}\left|l(S^1,A^1,\psi^1,\varphi^1,R^1,T^1)\right| &\leq \|f_1\|_2 \left\|S^1\right\|_2 + \|f_2\|_2 \left\|A^1\right\|_2 + \|f_3\|_2 \left\|\psi^1\right\|_2\\ &+ \|f_4\|_2 \left\|\varphi^1\right\|_2 + \|f_5\|_2 \left\|R^1\right\|_2 + \|f_6\|_2 \left\|T^1\right\|_2,\end{aligned}$$

then, for $M_3 > 0$:

$$\left|l(S^1,A^1,\psi^1,\varphi^1,R^1,T^1)\right| \leq M_3 \left\|(S^1,A^1,\psi^1,\varphi^1,R^1,T^1)\right\|_V. \tag{3.5}$$

As a result, the bilinear form b and the linear form l are continuous.
Moreover, for: $(S,A,\psi,\varphi,R,T) \in V$:

$$\begin{aligned}b\left((S,A,\psi,\varphi,R,T);(S,A,\psi,\varphi,R,T)\right) &= d_S \int_\Omega S^2 dx + d_S \int_\Omega \nabla S^2 dx\\ &+ d_2 \int_\Omega A^2 dx + d_2 \int_\Omega \nabla A^2 dx\\ &+ d \int_\Omega \psi^2 dx + d \int_\Omega \nabla \psi^2 dx\\ &+ d \int_\Omega \varphi^2 x + d \int_\Omega \nabla \varphi^2 dx\\ &+ d_R \int_\Omega R^2 dx + d_R \int_\Omega \nabla R^2 dx\\ &+ k \int_\Omega T^2 dx + k \int_\Omega \nabla T^2 dx,\\ &\geq d_S \left(\|S\|^2_{L^2_*(\Omega)} + \|\nabla S\|^2_{L^2_*(\Omega)}\right)\\ &+ d_2 \left(\|A\|^2_{L^2_*(\Omega)} + \|\nabla A\|^2_{L^2_*(\Omega)}\right)\\ &+ d \left(\|\psi\|^2_{L^2_*(\Omega)} + \|\nabla \psi\|^2_{L^2_*(\Omega)}\right)\\ &+ d \left(\|\varphi\|^2_{L^2_*(\Omega)} + \|\nabla \varphi\|^2_{L^2_*(\Omega)}\right)\\ &+ d_R \left(\|R\|^2_{L^2_*(\Omega)} + \|\nabla R\|^2_{L^2_*(\Omega)}\right)\\ &+ k \left(\|T\|^2_{L^2_*(\Omega)} + \|\nabla T\|^2_{L^2_*(\Omega)}\right).\end{aligned}$$

Then, for $M_4 > 0$

$$\begin{aligned}b\left((S,A,\psi,\varphi,R,T);(S,A,\psi,\varphi,R,T)\right) &\geq M_4(\|S\|^2_{H^1_*(\Omega)} + \|A\|^2_{H^1_*(\Omega)} + \|\psi\|^2_{H^1_*(\Omega)} + \|\varphi\|^2_{H^1_*(\Omega)}\\ + \|R\|^2_{H^1_*(\Omega)} + \|T\|^2_{H^1_*(\Omega)}) &\geq M_4 \left\|(S,A,\psi,\varphi,R,T)\right\|^2_V, \quad M_4 > 0.\end{aligned}$$

Hence, b is coercive.

So, by the Lax-Milgram theorem, there exists a unique solution $\Phi \in V$, satisfying:

$$\begin{aligned} b\left((S,A,\psi,\varphi,R,T);(S^1,A^1,\psi^1,\varphi^1,R^1,T^1)\right) &= L\left(S^1,A^1,\psi^1,\varphi^1,R^1,T^1\right); \\ \forall(S,A,\psi,\varphi,R,T) &\in V. \end{aligned}$$

Regularity:

Once the weak solution $\Phi \in V$ is established, we apply elliptic regularity theory for systems. The operator $I - A$ is elliptic, and the terms $f \in X$. From elliptic regularity theory, we conclude that $\Phi \in \left[H^2_*(\Omega)\right]^6$, provided the domain Ω is C^2 and the boundary conditions are smooth. Then, the regularity result provides the estimate:

$$\|\Phi\|_{[H^2_*(\Omega)]^4} \leq c \|f\|_X ,$$

where $c > 0$ depends on Ω and the coefficients d_u, d_2, d, d_R, k.

As a result, $(I - A)$ is surjective. We conclude, using the Lumer-Phillips theorem, that A is the infinitesimal generator of a linear C_0-semigroup on H.

Now, we prove that $F(\Phi)$ is Lipschitz. We need to show that there exists a constant $L > 0$ such that for any $\zeta, \chi \in X$, where $\zeta = (S, A, \psi, \varphi, R, T)$ and $\chi = \left(\tilde{S}, \tilde{A}, \tilde{\psi}, \tilde{\varphi}, \tilde{R}, \tilde{T}\right)$,

$$\|F(\zeta) - F(\chi)\|_X \leq L \|\zeta - \chi\|_X ,$$

$F(\zeta) - F(\chi)$ is given by:

$$F_1(\zeta) - F_1(\chi) = -\left[k_1(T)\frac{S}{k_2+S}(\psi+\varphi) - k_1(\tilde{T})\frac{\tilde{S}}{k_2+\tilde{S}}(\tilde{\psi}+\tilde{\varphi})\right],$$

$$\begin{aligned} F_2(\zeta) - F_2(\chi) &= -\left[\gamma(T)A - \gamma(\tilde{T})\tilde{A}\right] + \left[\alpha(T)\frac{RA}{K_L+RA}\psi - \alpha(\tilde{T})\frac{\tilde{R}\tilde{A}}{K_L+\tilde{R}\tilde{A}}\tilde{\psi}\right] \\ &\quad + \left[(\alpha(T)+\beta(T))\frac{RA}{K_L+RA}\varphi - \left(\alpha(\tilde{T})+\beta(\tilde{T})\right)\frac{\tilde{R}\tilde{A}}{K_L+\tilde{R}\tilde{A}}\tilde{\varphi}\right], \end{aligned}$$

$$\begin{aligned} F_3(\zeta) - F_3(\chi) &= k_3(T)\frac{S}{k_3+S}\psi - k_3(\tilde{T})\frac{\tilde{S}}{k_3+\tilde{S}}\tilde{\psi} + \left[k_5(T)A^m\psi - k_5(\tilde{T})\tilde{A}^m\tilde{\psi}\right] + [k_5(T)\varphi \\ &\quad -k_5(\tilde{T})\tilde{\varphi}] - \left[k_4(T)\psi - k_4(\tilde{T})\tilde{\psi}\right], \end{aligned}$$

$$\begin{aligned} F_4(\zeta) - F_4(\chi) &= k_3(T)\frac{S}{k_3+S}\varphi - k_3(\tilde{T})\frac{\tilde{S}}{k_3+\tilde{S}}\tilde{\varphi} + \left[k_5(T)A^m\psi - k_5(\tilde{T})\tilde{A}^m\tilde{\psi}\right] - \\ &\quad \left[k_5(T)\psi - k_5(\tilde{T})\tilde{\psi}\right] + \left[k_4(T)\varphi - k_4(\tilde{T})\tilde{\varphi}\right], \end{aligned}$$

$$\begin{aligned} F_5(\zeta) - F_5(\chi) &= -\left[k_R(T)R - k_R(\tilde{T})\tilde{R}\right] + \left[k_3(T)\frac{RA}{k_R+RA} - k_3(\tilde{T})\frac{\tilde{R}\tilde{A}}{k_R+\tilde{R}\tilde{A}}\right] \\ &\quad - \left[k_3(T)\frac{\psi+\varphi}{k_2+\psi+\varphi}R - k_3(\tilde{T})\frac{\tilde{\psi}+\tilde{\varphi}}{k_2+\tilde{\psi}+\tilde{\varphi}}\tilde{R}\right], \end{aligned}$$

$$F_6(\zeta) - F_6(\chi) = Q_0\left[\psi + \varphi - \tilde{\psi} - \tilde{\varphi}\right].$$

For $F_1(\zeta) - F_1(\chi)$, we have:

$$\begin{aligned} F_1(\zeta) - F_1(\chi) &= -[\left(k_1(T) - k_1(\tilde{T})\right)\frac{S}{k_2+S}(\psi+\varphi) - k_1(\tilde{T})[\frac{S}{k_2+S}(\psi+\varphi) \\ &\quad -k_1(\tilde{T})\frac{\tilde{S}}{k_2+\tilde{S}}(\tilde{\psi}+\tilde{\varphi})]], \end{aligned}$$

$$\begin{aligned} |F_1(\zeta) - F_1(\chi)| &\leq \left|k_1(T) - k_1(\tilde{T})\right| \left|\frac{S}{k_2+S}(\psi+\varphi)\right| \\ &+ \left|k_1(\tilde{T})\right| \left|\frac{S}{k_2+S}(\psi+\varphi) - \frac{\tilde{S}}{k_2+\tilde{S}}(\tilde{\psi}+\tilde{\varphi})\right|, \end{aligned}$$

then, there exists a constant L_{k_1} such that:

$$\left|k_1(T) - k_1(\tilde{T})\right| \leq L_{k_1}\left|T-\tilde{T}\right|,$$

we find the following estimations:

$$\left|\frac{S}{k_2+S}(\psi+\varphi) - \frac{\tilde{S}}{k_2+\tilde{S}}(\tilde{\psi}+\tilde{\varphi})\right| \leq \left|\frac{S}{k_2+S} - \frac{\tilde{S}}{k_2+\tilde{S}}\right| |\psi+\varphi| + \frac{|\tilde{S}|}{k_2+|\tilde{S}|}\left|(\psi+\varphi)-(\psi'+\varphi')\right|.$$

Also, on a bounded set, the function

$$g(s) = \frac{S}{k_2+S}$$

is continuously differentiable, therefore Lipschitz and bounded. Then, the product $\frac{S}{k_2+S}$ is Lipschitz in its variables when S, ψ, and φ remain bounded. Thus, there exists a constant L_1 such that:

$$\left|\frac{S}{k_2+S}(\psi+\varphi) - \frac{\tilde{S}}{k_2+\tilde{S}}(\tilde{\psi}+\tilde{\varphi})\right| \leq L_1\left(\left|S-\tilde{S}\right| + \left|\psi-\tilde{\psi}\right| + |\varphi-\tilde{\varphi}|\right),$$

Moreover, the term $\frac{S}{k_2+S}(\psi+\varphi)$ is bounded by a constant C_1 on the bounded set B.
Thus, we get:

$$\begin{aligned} |F_1(\zeta) - F_1(\chi)| &\leq L_{k_1}C_1\left|T-\tilde{T}\right| \\ &+L_1\left|k_1(\tilde{T})\right|\left(\left|S-\tilde{S}\right| + \left|\psi-\tilde{\psi}\right| + |\varphi-\tilde{\varphi}|\right), \end{aligned} \tag{3.6}$$

since on the bounded set the values of $\left|k_1(\tilde{T})\right|$ and C_1 are bounded, we can write:

$$\begin{aligned} |F_1(\zeta) - F_1(\chi)| &\leq L_{f_1}(\left|T-\tilde{T}\right| + \left|S-\tilde{S}\right| \\ &+ \left|\psi-\tilde{\psi}\right| + |\varphi-\tilde{\varphi}|), \end{aligned} \tag{3.7}$$

for $L_{f_1} > 0$.

Then, following a similar procedure, we find:

$$\begin{aligned} |F_2(\zeta) - F_2(\chi)| &\leq L_{f_2}(\left|T-\tilde{T}\right| + \left\|A-\tilde{A}\right\|_{L^\infty} \\ &+ \left\|\psi-\tilde{\psi}\right\|_{L^\infty} + \|\varphi-\tilde{\varphi}\|_{L^\infty}), \end{aligned} \tag{3.8}$$

where L_{f_2} is a positive constant depending on the Lipschitz constants of $\alpha(T)$, $\beta(T)$, and $\gamma(T)$, and the terms $\frac{RA}{K_L+RA}$.
For $F_3(\Phi)$, it is treated similarly to $F_2(\Phi)$, we find:

$$\begin{aligned} |F_3(\zeta) - F_3(\chi)| &\leq L_{f_3}(\left|T-\tilde{T}\right| + \left\|A-\tilde{A}\right\|_{L^\infty} \\ &+ \left\|\psi-\tilde{\psi}\right\|_{L^\infty} + \|\varphi-\tilde{\varphi}\|_{L^\infty}), \end{aligned} \tag{3.9}$$

and

$$\begin{aligned} |F_4(\zeta) - F_4(\chi)| &\leq L_{f_4}(\left|T-\tilde{T}\right| + \left\|A-\tilde{A}\right\|_{L^\infty} \\ &+ \left\|\psi-\tilde{\psi}\right\|_{L^\infty} + \|\varphi-\tilde{\varphi}\|_{L^\infty}), \end{aligned} \tag{3.10}$$

$$|F_5(\zeta)-F_5(\chi)| \leq L_{f_5}(|T-\tilde{T}|+\|A-\tilde{A}\|_{L^\infty} + \|\psi-\tilde{\psi}\|_{L^\infty}+\|\varphi-\tilde{\varphi}\|_{L^\infty}), \tag{3.11}$$

Finally, for $F_6(\Phi)$, we have:

$$F_6(\zeta)-F_6(\chi)=Q_0\left(\psi+\varphi-\tilde{\psi}-\tilde{\varphi}\right),$$

we find

$$|F_6(\zeta)-F_6(\chi)| \leq L_{f_6}\left(\|\psi-\tilde{\psi}\|_{L^\infty}+\|\varphi-\tilde{\varphi}\|_{L^\infty}\right). \tag{3.12}$$

As results, from (3.7), (3.8), (3.9), (3.14), (3.11) and (3.12), we find

$$\|F(\zeta)-F(\chi)\|_X \leq L\|\zeta-\chi\|_X , \tag{3.13}$$

where L is a constant that depends on the Lipschitz constants of the functions $\alpha(T)$, $\beta(T)$, $\gamma(T)$, $k_3(T)$, $k_4(T)$, $k_5(T)$, $k_R(T)$, and the terms A^m, $\frac{S}{k_2+S}$, $\frac{RA}{K_L+RA}$.

Then, F is Lipschitz continuous on X.

As a result, the problem (1.2)-(1.3) has a unique mild solution Φ given by

$$\Phi(t)=U(t)\Phi_0+\int_0^t U(t-y)F(\Phi(y))dy,$$

where $U(t)$ is the C_0-semigroup generated by A.

We now need to prove the well-posedness of the second term, where we use the fixed-point theorem.

We define the operator G as

$$G(\delta(t))=U(t)\Phi_0+\int_0^{\bar{T}} U(t-y)F(\delta(y))dy,$$

we show that G maps a suitable function space into itself.

The function space $C\left(\left[0,\bar{T}\right];X\right)$ is:

$$C\left(\left[0,\bar{T}\right],X\right)=\left\{v\in\left[0,\bar{T}\right]\to X \text{ such that } v(t) \text{ continuous in } t\right\},$$

We want to show that if $v\in C\left(\left[0,\bar{T}\right],X\right)$, then $G(v)\in C\left(\left[0,\bar{T}\right],X\right)$.

Boundedness of $U(t)$:

The C_0-semigroup $U(t)$ satisfies:

$$\|U(t)\|_{L^2_*(\Omega)\to L^2_*(\Omega)} \leq Me^{wt}, \quad M>0.$$

So the semigroup is bounded for $t>0$. From the earlier proof, F is Lipschitz continuous in X.

Boundedness of $G(v)$: For $C\left(\left[0,\bar{T}\right],X\right)$, we have:

$$\|U(t)\Phi_0\|_X \leq Me^{wt}\|\Phi_0\|_X .$$

And

$$\left\|\int_0^T U(t-y)F(\delta(y))dy\right\|_X \leq \int_0^t \|U(t-y)\|_X \|F(\delta(y))\|_X dy,$$

since

$$\|F(\delta(y))\|_X \leq C\left(1+\|\delta(y)\|_X\right);$$

we have

$$\|U(t-y)F(\delta(y))\|_X \leq Me^{w(t-y)}\left(1+\|\delta(y)\|_X\right),$$

thus,

$$\left\| \int_0^{\bar{T}} U(t-y)F(\delta(y))dy \right\|_X \leq MC \int_0^{\bar{T}} e^{w(t-y)} \left(1 + \|\delta(y)\|_X\right) dx.$$

As a result, $G(\delta)$ is bounded in X.

We have that $U(t)\Phi_0$ is continuous in t since $U(t)$ is strongly continuous, and the integral term is also continuous due to the continuity of $\delta(y)$ and F.

Hence, $G(\delta) \in C\left(\left[0, \bar{T}\right], X\right)$.

Secondly, we prove that G is a contraction.

We consider $\delta_1, \delta_2 \in C\left(\left[0, \bar{T}\right], X\right)$. We need to show that:

$$\|G(\delta_1)(t) - G(\delta_2)(t)\|_X \leq ML \|\delta_1 - \delta_2\|_{C([0,T],X)}, \tag{3.14}$$

we have

$$\begin{aligned} \|G(\delta_1)(t) - G(\delta_2)(t)\|_X &\leq \int_0^{\bar{T}} \|U(t-y)\| \, \|F(\delta_1(y)) - F(\delta_2(y))\|_X \, dy \\ &\leq M \int_0^{\bar{T}} e^{w(t-y)} \|F(\delta_1(y)) - F(\delta_2(y))\|_X \, dy. \end{aligned}$$

However, since F is Lipschitz, we find:

$$\begin{aligned} \|G(\delta_1)(t) - G(\delta_2)(t)\|_X &\leq ML \int_0^{\bar{T}} e^{w(t-y)} \|\delta_1(y) - \delta_2(y)\|_X \, du \\ &\leq ML \|\delta_1 - \delta_2\|_{C([0,T],X)} \int_0^{\bar{T}} e^{w(t-y)} dy, \end{aligned}$$

where

$$\int_0^{\bar{T}} e^{w(t-y)} du = \begin{cases} \int_0^{\bar{T}} 1du = T, if \ w = 0 \\ \frac{1-e^{wt}}{w}, \ if \ w \neq 0 \end{cases},$$

Thus;

$$\|G(\delta_1)(t) - G(\delta_2)(t)\|_X \leq ML \|\delta_1 - \delta_2\|_{C\left(\left[0,\bar{T}\right],X\right)}.$$

For $\bar{T} > 0$ sufficiently small such that $ML\bar{T} < 1$, G is a contraction, ensuring a unique fixed point by the Banach Fixed-Point Theorem.

Remark 3.1 (Continuation beyond small time). Let $\bar{T} > 0$ be the small time for which the contraction $ML\bar{T} < 1$ holds. Denote by $\Phi(t)$ the unique solution on $[0, \bar{T}]$. Since $\Phi(\bar{T})$ lies in the same Banach space, one may restart the contraction argument on $[\bar{T}, 2\bar{T}]$ with initial data $\Phi(\bar{T})$. By iterating this stepwise continuation, the solution extends uniquely to any finite time interval $[0, T_{\text{final}}]$.

3.2 Regularity of the solution:

If the initial condition $\Phi_0 \in D(A)$, the solution satisfies:

$$\frac{d\Phi}{dt} \in X; \ \Phi(t) \in D(A).$$

making $\Phi(t)$ a strong solution.

If $\Phi_0 \in H^k(\Omega)$ and F is smooth, the solution $\Phi(t)$ inherits higher regularity.

$$\Phi(t) \in H^k(\Omega), \ \ for \ t > 0.$$

3.3 Uniqueness

Uniqueness of the solution follows directly from the contraction mapping argument.

If there were two solutions $\Phi_1(t)$ and $\Phi_2(t)$ that satisfy:

$$\frac{d}{dt}\left(\Phi_1-\Phi_2\right)=A\left(\Phi_1-\Phi_2\right)+F\left(\Phi_1\right)-F\left(\Phi_2\right),$$

Using the Lipschitz property of F, this leads to:

$$\left\|\Phi_1(t)-\Phi_2(t)\right\|_X \leq L\bar{T}\left\|\Phi_1-\Phi_2\right\|_{C\left(\left[0,\bar{T}\right],X\right)},$$

where $\bar{T}L<1$, hence $\Phi_1(t)=\Phi_2(t)$.

This completes the proof of existence, uniqueness, and regularity of the solution of (1.2)-(1.3).

4 Numerical Approximation

In this section, we propose a numerical approximation of the nonlinear system of partial differential equations described in the previous section. We discretize the system in space using finite elements and in time using an implicit Euler scheme.

Start with the weak formulation. Multiply equations $(1.2)_1$, $(1.2)_2$, $(1.2)_3$, $(1.2)_4$, $(1.2)_5$, $(1.2)_6$ by $v^S, v^A, v^\psi, v^\varphi, v^R$, and v^T respectively, then integrate over Ω, and using integration by parts, we get the following weak formulation:

find $(S,A,\psi,\varphi,R,T)\in\left(H_*^1(\Omega)\right)^6$, such that $\forall\left(v^S,v^A,v^\psi,v^\varphi,v^R,v^T\right)\in\left(H_*^1(\Omega)\right)^6$,

$$\left\{\begin{array}{l}
\int\limits_{\Omega_T}\frac{\partial S}{\partial t}v^S dx+d_s\int\limits_{\Omega_T}\nabla S\nabla v^S dx=\int\limits_{\Omega_T}k_1(T)\,g(S,\psi+\varphi)v^S dx\\
\int\limits_{\Omega_T}\frac{\partial A}{\partial t}v^A dx+d_2\int\limits_{\Omega_T}\nabla A\nabla v^A dx+\int\limits_{\Omega_T}\gamma(T)\,Av^A dx=\int\limits_{\Omega_T}\alpha(T)\,\frac{RA}{K_L+RA}\psi v^A dx+\\
\int\limits_{\Omega_T}\left(\alpha(T)+\beta(T)\right)\frac{RA}{K_L+RA}\varphi v^A dx\\
\int\limits_{\Omega_T}\frac{\partial\psi}{\partial t}v^\psi dx+d\int\limits_{\Omega_T}\nabla\psi\nabla v^\psi dx+\int\limits_{\Omega_T}k_5(T)\left|A\right|^m\psi v^\psi dx=\int\limits_{\Omega_T}\left(k_3(T)\,g(S,\psi)+k_5(T)\,\varphi\right)v^\psi dx\\
\int\limits_{\Omega_T}\frac{\partial\varphi}{\partial t}v^\varphi dx+d\int\limits_{\Omega_T}\nabla\varphi\nabla v^\varphi+\int\limits_{\Omega_T}\left(k_4(T)+k_5(T)\right)\varphi v^\varphi dx=\int\limits_{\Omega_T}\left(k_3(T)\,g(S,\varphi)+k_5(T)\left|A\right|^m\psi\right)v^\varphi dx\\
\int\limits_{\Omega_T}\frac{\partial R}{\partial t}v^R dx+d_R\int\limits_{\Omega_T}\nabla R\nabla v^R dx+\int\limits_{\Omega_T}k_R(T)\,Rv^R dx+\int\limits_{\Omega_T}k_3(T)\,g(\psi+\varphi,R)v^R dx\\
=\int\limits_{\Omega_T}k_3(T)\,\frac{RA}{k_R+RA}v^R dx\\
\int\limits_{\Omega_T}\frac{\partial T}{\partial t}v^T dx+k\int\limits_{\Omega_T}\nabla T\nabla v^T dx=\int\limits_{\Omega_T}Q_0(\psi+\varphi)v^T dx
\end{array}\right. . \tag{4.1}$$

Then, let $0=t_0<t_1<...<t_{N-1}<t_N$ be a partitioning of $\left[0;\bar{T}\right]$ into variable time steps $\tau_n=t_n-t_{n-1}, n=1,...,N$. We set $\tau=\max_{1\leq n\leq N}$. We introduce $\left(\lambda_h\right)_h$ a shape-regular family of triangulations of Ω. For a triangle $k\in\lambda_h$, let h_k be its diameter and set $h=\max_{k\in T_h}h_k$. For any subdomain w of Ω we define by $P^1(w)$ the space of polynomials on w with degree ≤ 1. We denote by $(.,.)_w$ the usual L^2 product on w and by $\|.\|_w$ the associated norm. Furthermore, we denote by $|.|_{1,w}$ the semi-norm on $H^1(w)$. For ease of notation, when $w=\Omega$ we drop the subscript,

$$P^1(\lambda_h)=\left\{v_h\in C^0(\Omega),\forall k\in\lambda_h,v_h/k\in P^1(k)\right\},$$

$$P_\beta^1(\lambda_h)=\left\{v_h\in P^1(\lambda_h),v_h\geq 0\right\},$$

$$P_{1,SD}(\mathcal{T}_h)=\{v_h\in P_1(\mathcal{T}_h):v_h|_{\Gamma_D}=0\},$$

and we set

$$w_h=\left\{v_h\in P^1(\lambda_h),v_h\geq 0\right\},$$

and

$$w_h^\beta = \left\{ v_h \in P^1(\lambda_h), v_h \geq 0 \right\},$$

we consider the problem: For $(S_h^n, A_h^n, \psi_h^n, \varphi_h^n, R_h^n, T_h^n) \in P^1(\lambda_h) \times P^1_{S_D}(\lambda_h) \times P^1(\lambda_h) \times P^1(\lambda_h) \times P^1(\lambda_h) \times P^1(\lambda_h)$, we seek

$$\begin{aligned}\left(S_h^{n+1}, A_h^{n+1}, \psi_h^{n+1}, \varphi_h^{n+1}, R_h^{n+1}, T_h^{n+1}\right) \quad \in \quad & P^1(\lambda_h) \times P^1_{S_D}(\lambda_h) \\ & \times P^1(\lambda_h) \times P^1(\lambda_h) \times P^1(\lambda_h) \times P^1(\lambda_h)\end{aligned}$$

such that, for all $\left(v_h^S, v_h^A, v_h^\psi, v_h^\varphi, v_h^R, v_h^T\right) \in P_0^1(\lambda_h) \times P^1(\lambda_h) \times P^1(\lambda_h)$ $\times P^1(\lambda_h) \times P^1(\lambda_h) \times P^1(\lambda_h)$

$$\begin{cases}
\int\limits_{\Omega_T} \frac{(S_h^{n+1}-S_h^n)}{\tau_n} v_h^S dx + \int\limits_{\Omega_T} \left[d_s \nabla S_h^{n+1} . \nabla v_h^S + k_1(T_h^n) g(S_h^{n+1}, \psi_h^n + \varphi_h^n) v_h^S \right] dx = 0 \\
\int\limits_{\Omega_T} \frac{A_h^{n+1}-A_h^n}{\tau_n} v_h^A dx + \int\limits_{\Omega_T} \left[d_2 \nabla A_h^{n+1} \nabla v_h^A dx + \gamma(T_h^n) A_h^{n+1} v_h^A \right] dx = \int\limits_{\Omega_T} \alpha(T_h^n) \frac{R_h^n A_h^{n+1}}{K_L + R_h^n A_h^{n+1}} \psi_h^n v_h^A dx \\
+ \int\limits_{\Omega_T} \left(\alpha(T_h^n) + \beta(T_h^n)\right) \frac{R_h^n A_h^{n+1}}{K_L + R_h^n A_h^{n+1}} \varphi_h^n v_h^A dx \\
\int\limits_{\Omega_T} \frac{\psi_h^{n+1}-\psi_h^n}{\tau_n} v_h^\psi dx + \int\limits_{\Omega_T} \left[d \nabla \psi_h^{n+1} \nabla v_n^\psi dx + k_5(T_h^n) \left|A_h^{n+1}\right|^m \psi_h^{n+1} v_h^\psi \right] dx = \int\limits_{\Omega_T} (k_3(T_h^n) g\left(S_h^{n+1}, \psi_h^n\right) \\
+ k_5(T_h^n) \varphi_h^n) v_h^\psi dx \\
\int\limits_{\Omega_T} \frac{\varphi_h^{n+1}-\varphi_h^n}{\tau_n} v_h^\varphi dx + \int\limits_{\Omega_T} \left[d \nabla \varphi_h^{n+1} \nabla v_h^\varphi + (k_4(T_h^n) + k_5(T_h^n)) \varphi_h^{n+1} v_h^\varphi \right] dx \\
= \int\limits_{\Omega_T} \left(k_3(T_h^n) g(S_h^{n+1}, \varphi_h^{n+1}) + k_5(T_h^n) \left|A_h^{n+1}\right|^m \psi_h^{n+1} \right) v_h^\varphi dx \\
\int\limits_{\Omega_T} \frac{R_h^{n+1}-R_h^n}{\tau_n} v_h^R dx + \int\limits_{\Omega_T} \left[d_R \nabla R_h^{n+1} \nabla v_h^R + k_R(T_h^n) R_h^{n+1} v_h^R + k_3(T_h^n) g(\psi_h^{n+1} + \varphi_h^{n+1}, R_h^{n+1}) v_h^R \right] dx \\
= \int\limits_{\Omega_T} k_3\left(T_h^{n+1}\right) \frac{R_h^{n+1} A_h^{n+1}}{k_R + R_h^{n+1} A_h^{n+1}} v_h^R dx \\
\int\limits_{\Omega_T} \frac{T_h^{n+1}-T_h^n}{\tau_n} v_h^T dx + \int\limits_{\Omega_T} \left[k \nabla T_h^{n+1} \nabla v_h^T \right] dx = \int\limits_{\Omega_T} Q_0(\psi_h^{n+1} + \varphi_h^{n+1}) v_h^T dx
\end{cases}, \tag{4.2}$$

Theorem 4.1. *Let* $(S_h^n, A_h^n, \psi_h^n, \varphi_h^n, R_h^n, T_h^n) \in w_h^{S_D} \times w_h \times w_h \times w_h \times w_h \times w_h$. *Then for all* h, $\tau_n > 0$, *there exists a unique solution* $\left(S_h^{n+1}, A_h^{n+1}, \psi_h^{n+1}, \varphi_h^{n+1}, R_h^{n+1}, T_h^{n+1}\right) \in w_h^{S_D} \times w_h \times w_h \times w_h \times w_h \times w_h$.

Proof. We denote by $\{\gamma_i\}_{1 \leq i \leq N}$ the usual basis functions of $P_0^1(T_h)$. For any

$$w = \sum_{j=1}^{j=N} w_j \gamma_j \in P_0^1(\lambda_h),$$

we define $\tilde{w} = (w_1, w_2, ..., w_N)^T \in \mathbb{R}^N$. We then set $F_s^n : \mathbb{R}^N \times \mathbb{R}^N \to \mathbb{R}^N$ we define by:

$$\left[F_s^n(\tilde{w}, \tilde{z})\right]_j = (w, \gamma_j) + \tau_n d(\nabla w, \nabla \gamma_j) + \tau_n (f(w) z, \gamma_j), \quad j = 1, ...N.$$

For S^n and ψ^n given in W_h and W_h^0 respectively, we write the first equation of (P_h), where $d = d_S$, as:

$$F_s^n\left(\tilde{S}^{n+1}, \tilde{\psi}^n + \tilde{\varphi}^n\right) = \tilde{G}_s^n \in \mathbb{R}^N_{\geq 0},$$

with $\left[\tilde{G}_s^n\right]_j = (S^n, \gamma_j)$. One can prove that, for every fixed $z \in \mathbb{R}^N$, we have that $F_s^n(., z) : \mathbb{R}^N \to \mathbb{R}^N$ is an isotone homeomorphism. We refer to [15] for more details, and from $F_s^n\left(\tilde{0}, \tilde{\psi}^n\right) = \tilde{0}$, we deduce the existence and uniqueness solution S_h^n in W_h solving the ferst equation of (λ_h).

In the same way we prove the existence and uniqueness of $(A_h^n, \psi_h^n, \varphi_h^n, R_h^n, T_h^n) \in (w_h)^5$. For any $z_h^{n+1} \in W$, we set

$$F\left(z^{n+1}\right) = \sum_{n=1}^{N} \tau_n \left|\frac{z^{n+1} - z^n}{\tau_n}\right|^2 + \max_n \left|z^{n+1}\right|_1^2 + \sum_{n=1}^{N} \tau_n \left|z^{n+1} - z^n\right|_1^2.$$

□

Lemma 4.2. *For all $h > 0$ and for all time paratitions $\{\tau_n\}_n$, the solution $(S_h^n, A_h^n, \psi_h^n, \varphi_h^n, R_h^n, T_h^n)$ of (P_h) satisfies*

$$\begin{aligned} & F\left(S_h^{n+1}\right) + F\left(A_h^{n+1}\right) + F\left(\psi_h^{n+1}\right) + F\left(\varphi_h^{n+1}\right) + F\left(R_h^{n+1}\right) \\ +F\left(T_h^{n+1}\right) \quad \leq \quad & C(\left|S_h^0\right|_1^2 + \left|A_h^0\right|_1^2 + \left|\psi_h^0\right|_1^2 \\ & + \left|\varphi_h^0\right|_1^2 + \left|R_h^0\right|_1^2 + \left|T_h^0\right|_1^2 + C). \end{aligned}$$

The above bound is obtained by using $z^{n+1} - z^n$ as test function in each equation of (P_h). Here z_h^n denotes arbitrarily $S_h^n, A_h^n, \psi_h^n, \varphi_h^n, R_h^n$ or v_h^n.

Let us now state that the solution of the numerical scheme converges to a weak solution of (P_h). We set $\Omega_T = \Omega \times (0, T)$ and we introduce the following notation

$$z(t) = \frac{t - t^n}{\tau_n} z^{n+1} + \frac{t^{n+1} - t}{\tau_n} z^n, \; t \in \left[t^n, t^{n+1}\right], n \geq 1,$$

and

$$z^+(t) = z^{n+1}, z^-(t) = z^n, \; t \in \left[t^n, t^{n+1}\right], n \geq 1.$$

Using this notation the problem (P_h) reads as: Seek

$$(S_h^n, A_h^n, \psi_h^n, \varphi_h^n, R_h^n, T_h^n) \in \left[C^0\left([0, T] \times W_h\right)\right]^6,$$

such that

$$\begin{cases} \int\limits_{\Omega_T} \frac{\partial S_h}{\partial t} v_h^S dx + d_s \int\limits_{\Omega_T} \nabla S_h \nabla v_h^S dx = \int\limits_{\Omega_T} k_1\left(T_h\right) g(S_h, \psi_h + \varphi_h) v_h^S dx \\ \int\limits_{\Omega_T} \frac{\partial A_h}{\partial t} v_h^A dx + d_2 \int\limits_{\Omega_T} \nabla A_h \nabla v_h^A dx + \int\limits_{\Omega_T} \gamma\left(T_h\right) A v_h^A dx = \int\limits_{\Omega_T} \alpha\left(T_h\right) \frac{R_h A_h}{K_L + R_h A_h} \psi_h v_h^A dx + \\ \int\limits_{\Omega_T} \left(\alpha\left(T_h\right) + \beta\left(T_h\right)\right) \frac{R_h A_h}{K_L + R_h A_h} \varphi_h v_h^A dx \\ \int\limits_{\Omega_T} \frac{\partial \psi_h}{\partial t} v_h^\psi dx + d \int\limits_{\Omega_T} \nabla \psi_h \nabla v_h^\psi dx + \int\limits_{\Omega_T} k_5\left(T_h\right) \left|A_h\right|^m \psi_h v_h^\psi dx = \int\limits_{\Omega_T} (k_3\left(T_h\right) g\left(S_h, \psi_h\right) \\ + k_5\left(T_h\right) \varphi_h) v_h^\psi dx \\ \int\limits_{\Omega_T} \frac{\partial \varphi_h}{\partial t} v_h^\varphi dx + d \int\limits_{\Omega_T} \nabla \varphi_h \nabla v_h^\varphi + \int\limits_{\Omega_T} (k_4\left(T_h\right) + k_5\left(T_h\right)) \varphi_h v_h^\varphi dx \\ = \int\limits_{\Omega_T} \left(k_3\left(T_h\right) g(S_h, \varphi_h) + k_5\left(T_h\right) \left|A_h\right|^m \psi_h\right) v_h^\varphi dx \\ \int\limits_{\Omega_T} \frac{\partial R_h}{\partial t} v_h^R dx + d_R \int\limits_{\Omega_T} \nabla R_h \nabla v_h^R dx + \int\limits_{\Omega_T} k_R\left(T_h\right) R_h v_h^R dx + \int\limits_{\Omega_T} k_3\left(T_h\right) g(\psi_h + \varphi_h, R_h) v_h^R dx = \\ \int\limits_{\Omega_T} k_3\left(T_h\right) \frac{R_h A_h}{k_R + R_h A_h} v_h^R dx \\ \int\limits_{\Omega_T} \frac{\partial T_h}{\partial t} v_h^T dx + k \int\limits_{\Omega_T} \nabla T_h \nabla v_h^T dx = \int\limits_{\Omega_T} Q_0(\psi_h + \varphi_h) v_h^T dx \end{cases}.$$

On introducing

$$\chi(z) = \left\|z^\pm\right\|_{L^\infty(\Omega_T)}^2 + \left\|z^\pm\right\|_{L^\infty(0,T,H^1(\Omega))}^2 + \left\|\frac{\partial z}{\partial t}\right\|_{L^2(\Omega_T)}^2 + \tau^{-1} \left\|z^+ - z^-\right\|_{L^2(0,T,H^1(\Omega))}^2,$$

where $z^\pm$ is an abbreviation for "with" and "without" corresponding to the superscripts "+" and "-", the lemma yields that:

$$\chi\left(S_h\right) + \chi\left(A_h\right) + \chi\left(\psi_h\right) + \chi\left(\varphi_h\right) + \chi\left(R_h\right) + \chi\left(T_h\right) \leq C(T).$$

In the following $z_h = S_h, A_h, \psi_h, \varphi_h, R_h$ or T_h and $z = S, A, \psi, \varphi, R$ or T.

From the last inequality, we infer the convergence result stated in the lemma below:

Lemma 4.3. *Let us assume that there is a constant $C > 0$ such that $\tau h < C$. Then, there exists a subsequence $\{z\}_h$ and a function $z \in L^\infty(\Omega_T) \cap H^1(0, T, L^2(\Omega))$ such that as $h \to 0$*

$$\begin{aligned} z, z^\pm &\to z \text{ weak- in } L^\infty(\Omega_T), \\ \frac{\partial z}{\partial t} &\to \frac{\partial z}{\partial t} \text{ weakly } L^2(\Omega_T), \\ z, z^\pm &\to z \text{ weak- in } L^\infty(0, T, H^1(\Omega)), \\ z, z^\pm &\to z \text{ strongly in } L^2(\Omega_T) \text{ and in } \Omega_T. \end{aligned}$$

Theorem 4.4. *Under the assumption of last lemma, and $z_0 \in H^2(\Omega)$, the solution of (4.2) converges to the solution of the weak form (4.1) of the system (1.2)-(1.3).*

4.1 Numerical Results

We consider the computational domain $\Omega_{\bar{T}} = [0, 1] \times [0, 0.5] \times [0, 20]$. The boundary Γ_D is the part on which the substrate and the antibiotics are applied.

At $t = 0$ the biofilm domain is defined by $\Omega_b(0) = \{(x_1, x_2) \in \Omega; x_2 \geq 0, x_1^2 + x_2^2 = 0.01\}$ and contained down-regulated biomass only.

Dimensionless model parameters used in the system (1.2)-(1.3), adapted from [19]. We take the values of the constants as follows:

$$\begin{aligned} &m = 2.5, \quad d = 1e - 7, \quad d_S = 1.67, \\ &d_R = 0.1, \quad d_2 = 12.9 \quad q_0 = 0.1, \\ &k = 0.1. \end{aligned}$$

In Figure1 we show the spatial distribution of down-regulated and up-regulated cells at times $t = 10$ and $t = 15$. The top row shows the case with no antibiotic or QSB agent applied, the middle row the case where only antibiotic is applied, and the bottom row the case where both antibiotic and QSB agent act. One observes how the antibiotic and QSB agent reduce the quantity of bacteria and modify their spatial expansion in the presence of heat effects.

The numerical results we present below concern the evolution of each variable with respect to time. We set:

$$\begin{aligned} \psi_{Total}(t) &= \frac{1}{|\Omega|} \int_\Omega \psi(x, t) dx, \quad \varphi_{Total}(t) = \frac{1}{|\Omega|} \int_\Omega \varphi(x, t) dx, \\ A_{Total}(t) &= \frac{1}{|\Omega|} \int_\Omega A(x, t) dx, \quad R_{Total}(t) = \frac{1}{|\Omega|} \int_\Omega R(x, t) dx, \\ T_{Total}(t) &= \frac{1}{|\Omega|} \int_\Omega T(x, t) dx. \end{aligned}$$

The quantity of antibiotic applied at the top of the domain is $V_D = 10$, and the quantity of QSB agent applied at the top of the domain, Γ_D, is $Q_D = 10$.

In Figure2, we plot the evolution of the down-regulated and up-regulated cells with respect to time. Then Figure3 presents the total amounts of ψ and φ with respect to time: without antibiotic and QSB, with antibiotic, with QSB, and with antibiotic and QSB. Finally, Figure4 shows Temperature distribution at t = 15 h under antibiotic + QSB treatment.

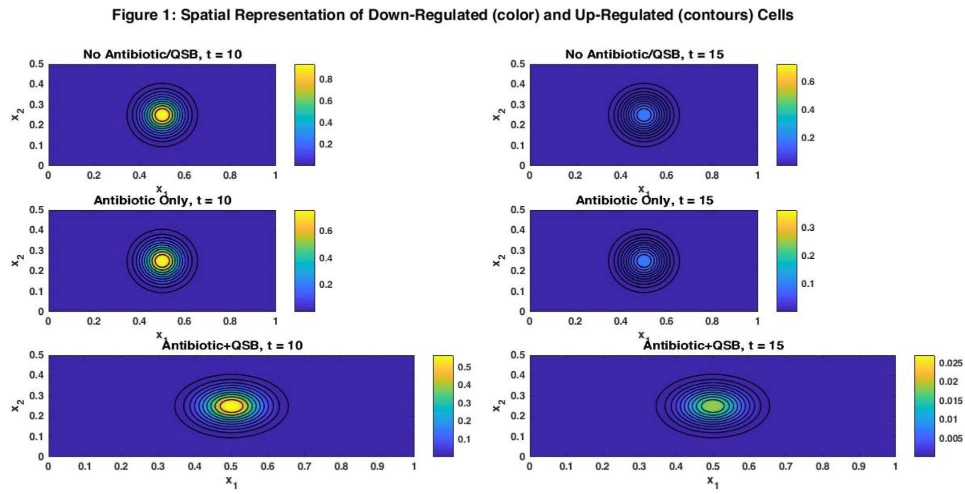

Figure 1. Representation of down-regulated and up-regulated cells at time $t = 10$ and $t = 15$.

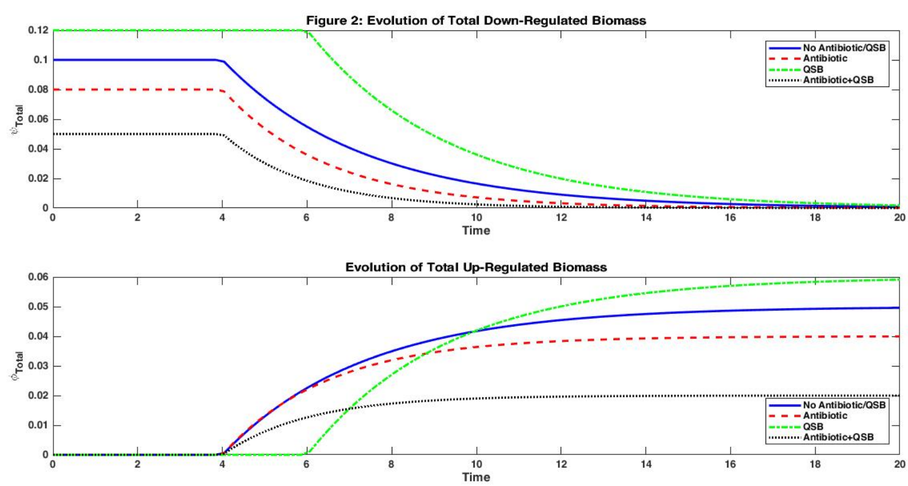

Figure 2. Total amounts of down-regulated and up-regulated cells with respect to time.

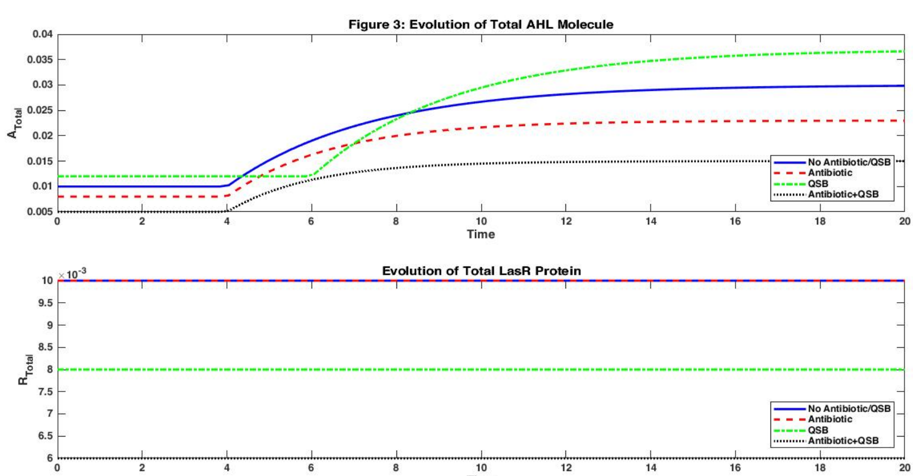

Figure 3. Evolution of total AHL molecule and LasR protein.

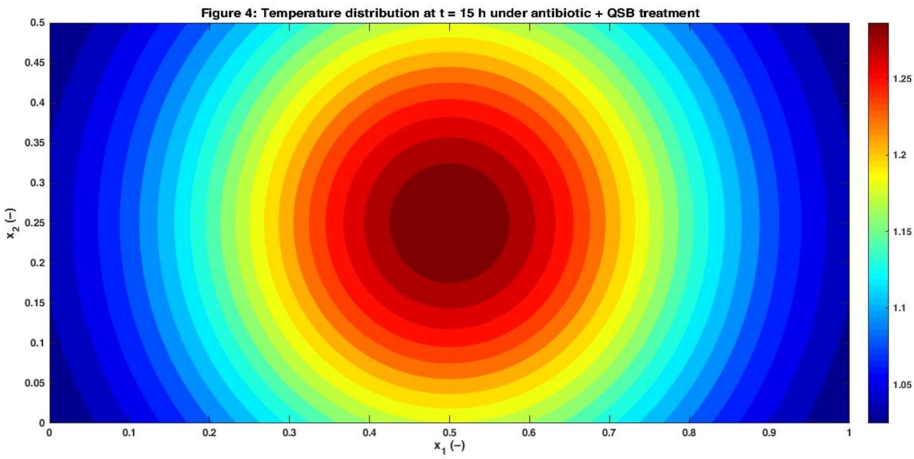

Figure 4. Temperature distribution at t = 15 h under antibiotic + QSB treatment.

5 Conclusion

We proposed and analyzed a nonlinear reaction-diffusion model that couples quorum sensing dynamics with heat transfer in bacterial biofilms. The model incorporates temperature-dependent reaction rates and metabolic heat generation, reflecting realistic biological behavior. We established the existence and uniqueness of solutions using semigroup theory and developed a finite element scheme to approximate the system numerically. The results of our simulations demonstrate the significant impact of temperature on quorum sensing activation, antibiotic effectiveness, and overall biofilm growth. These findings highlight the importance of considering thermal effects in the design and evaluation of bacterial treatment strategies.

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