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DRUG RELEASE ENHANCED BY TEMPERATURE: AN ACCURATE DISCRETE MODEL FOR SOLUTIONS IN H^3

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ABSTRACT: In this paper we consider the coupling between two quasilinear diffusion equations: the diffusion coefficient of the first equation depends on its solution and the diffusion and convective coefficients of the second equation depend on the solution of the first one. This system can be used to describe the drug evolution in a target tissue when the drug transport is enhanced by heat. We study, from an analytical and a numerical viewpoints, the coupling of the heat equation with the drug diffusion equation. A fully discrete piecewise linear finite method is proposed to solve this system and its stability is studied. Assuming that the heat and the concentration are in H^3 we prove that the method is second order convergent. Numerical experiments illustrating the theoretical results and the global qualitative behavior of the coupling are also included.

Keywords: Drug release, Temperature, Concentration, Piecewise linear finite element method, Finite differences, sharp-estimates, numerical simulation.

1. Introduction

In recent years advances in materials science and nanotechnology have given huge contributions to the development of drug delivery systems which represent an important tool in the framework of a precision medicine. The most challenging problems faced by researchers in the area are the development of systems for targeted release, controlled release or enhanced release. Targeted release refers to systems that deliver drugs to specific parts of the body, avoiding global systemic absorption. Examples of targeted delivery systems are polymeric intravitreal implants where the drug is dispersed or the use of nanoparticle drug carriers. When the drug targets the tissue or organ, the release is sustained when it is extended over a period of time to keep concentration levels within a therapeutic window. In the case of polymeric implants the release can be controlled by tuning the properties of the polymer and of the drug-polymer interactions. In some cases the delivery must be enhanced. To enhance drug release from drug delivery systems and also drug transport through the target tissue, chemical enhancers or physical

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enhancers as electric fields, magnetic fields, ultrasound, heat, are used nowadays. These stimuli are used individually or coupled in different areas, being oncology one of the most promising and challenging (see [5], [6], [12], [18] and [21])). In oncologic diseases the transport of the chemotherapy cocktails can be made by specific nanoparticles and the stimuli act to enhance the drug release from the transporter ([11], [14], [18], [20], [23]).

Another area of great application is transdermal delivery where it is crucial to enhance the permeability of the stratum corneum, the outermost layer of the epidermis. In this case external stimuli as heat, electric fields or ultrasounds have been used with great success (see for instance [4], [9], [11], [13], [15], [19] and [24]). Another important application of ultrasound, as an enhancer, is drug delivery to the brain where the stimulus act as a disruptor of the blood brain barrier ([12], [22]).

In the present paper we are mainly interested on drug delivery systems where the drug release is enhanced by the temperature. Heat has been used as enhancer in different situations as for instance in transdermal drug delivery. An increasing body of evidence suggests that temperature largely influences drug distribution, altering rate profile ([9]).

One popular application of heat in transdermal drug delivery are patches. We mention, for example patches where dispersed iron powder represent a heat source. Oxidation of the iron powder that generates an increase of the temperature that lead to an increase of permeability of the skin as well as a decrease in its Young modulus ([24]). Consequently, an increase in the drug flux through the skin is observed, and due to the increase of the superficial blood perfusion, an increase in the drug absorption occurs (see [15], [19]). Heat can be also generated by the application of other stimuli as ultrasounds [11] or electric fields [4].

When temperature increases, the pattern of Brownian motion is altered. In fact the *rate* of diffusion defined by the diffusion coefficient strongly depends on temperature. In the case of spherical particles through a liquid with low Reynolds number, the Stokes-Einstein equation postulates that the diffusion coefficient D is defined by

$$D = \frac{K_B T}{6\Pi \eta r},$$

where T denotes the temperature, K_B is the Boltzman constant, r the radius of a spherical drug molecule and η the viscosity.

The diffusion coefficient in solids at a specific temperature T is given by the Arrhenius equation

$$D = D_0 \exp\left(-\frac{E_{\mathrm{A}}}{RT}\right), \tag{1}$$

where D_0 is the maximal diffusion coefficient (at infinite temperature), E_A is the activation energy for diffusion, and R denotes the universal gas constant.

Heat is also generated as a consequence of the application of other physical enhancers as electric fields or ultrasound. We remark that electric fields have been used to enhance drug transport through the skin namely for electric charged drug molecules. In this case, a convective drug transport arises induced by the electric field defined by the gradient of the electric potential ([4]). The electric field generates heat that can be described by the Pennes' bioheat equation [16]

$$\rho k_s \frac{\partial T}{\partial t} = \nabla.(D_T \nabla T) - \omega_m c_b (T - T_a) + q + Q_J, \tag{2}$$

where T denotes the temperature, ρ represents the tissue density, k_s is the specific heat of the tissue,D_T is the thermal conductivity, T_a is the arterial blood temperature, q is the metabolic volumetric heat generation, ω_m is the nondirectional blood flow associated with perfusion, c_b is the specific heat of blood. In (2), Q_J denotes the heat generated by the applied potential ϕ that is given by $Q_J = \sigma |\nabla \phi|^2$, where σ is the electrical conductivity and $|.|$ represents the euclidian norm (see for instance [4]).

In the previous scenario, the drug molecules transport through the target tissue is described by the convection-diffusion-reaction equation

$$\frac{\partial c}{\partial t} - \nabla.\Big(\big(v_c \nabla \phi + w_F u_{eff}\big) c\Big) = \nabla.(D_d \nabla c), \tag{3}$$

where c denotes the drug concentration, D_d is the diffusion coefficient, v_c is the electrophoretic mobility coefficient which describes the ability of the electric field to move the solute, and u_{eff} is the electro-osmotic flow coefficient. The electrophoretic coefficient v_c is related with the diffusion coefficient via Einstein-Smoluchowski relation $v_c = D_d \dfrac{zF}{RT}$, where F is Faraday's number. In (3), w_F is a convective flow hindrance associated with a bulk convective flow with an average flow velocity u_{eff} (see [4]).

Our aim is to study the convection-diffusion-reaction equation for a drug concentration

$$\frac{\partial c}{\partial t} + \nabla.(v(T)c) = \nabla.(D_d(T)\nabla c) + Q(c) \text{ in } \Omega \times (0, T_f] \tag{4}$$

where T denotes the temperature defined by

$$\frac{\partial T}{\partial t} = \nabla.(D_T(T)\nabla T) + G(T) \text{ in } \Omega \times (0, T_f]. \tag{5}$$

In (4), $v(T)$ denotes the drug velocity and D_d is the diffusion coefficient. To describe the dependence of drug distribution on temperature, we assume that D_d in (4) is a function of the temperature T. We observe that equations (4) and (5) describe the drug evolution in two different situations: when heat is generated by a source term, like in heat patches applications, or when heat is generated as a secondary stimulus.

The concentration and temperature equations, (4) and (5), respectively, are complemented with homogeneous Dirichlet boundary conditions

$$c(t) = 0 \text{ on } \partial\Omega \times (0, T_f], T(t) = 0 \text{ on } \partial\Omega \times (0, T_f], \tag{6}$$

and initial conditions

$$c(0) = c_0 \text{ in } \Omega \times (0, T_f], T(0) = T_0 \text{ in } \Omega \times (0, T_f]. \tag{7}$$

To simplify, we assume that the medium Ω is isotropic which means that we can replace it by $\Omega = (0, 1)$.

Our aim is to propose a stable and accurate numerical method to compute numerical approximations for the temperature and concentration. The method is based on a piecewise linear finite element method combined with particular integration formulas. Such fully discrete method can be seen as a finite difference method defined on a nonuniform grid. We prove that the approximations for the temperature and concentration and their gradients are second order convergent with respect to discrete L^2-norms. It is well known that the piecewise linear finite element method (FEM) leads to first order approximations for the gradient. Such result shows the supercloseness of the gradient approximations. As we mentioned before, the fully discrete FEM is equivalent to a finite difference method defined on a nonuniform grid with first order truncation error with respect to the norm $\|.\|_\infty$. This result shows the supraconvergence of the method.

The paper is organized as follows. In Section 2 we study the stability of the continuous coupled model (4)-(5). The method proposed to solve numerically the coupled problem is introduced in Section 3. In this section, the stability of the method is established under certain conditions. In Section 4, an error analysis is developed which is not based on the use of the truncation error neither on the stability of the method. Numerical experiments illustrating the convergence results and the behaviour of the concentration and temperature are included in Section 5. Finally, in Section 6 we present some conclusions.

2. The continuous model: stability analysis

In this section we study the stability of the coupled problems (4)-(5). Let $c(t)$ and $T(t)$ in $L^2(0, T_f, H_0^1(\Omega))$ be such that

$$\begin{aligned}(T'(t), u) &= -(D_T(T)\nabla T(t), \nabla u) \\ &+(G(T), u) \text{ a.e. } (0, T_f], \forall u \in H_0^1(\Omega),\end{aligned} \tag{8}$$

and

$$\begin{aligned}(c'(t), w) - (v(T)c, \nabla w) &= -(D_d(T)\nabla c, \nabla w) \\ &+(Q(c), w) \text{ a.e. } (0, T_f], \forall w \in H_0^1(\Omega).\end{aligned} \tag{9}$$

In (8) and (9), $(.,.)$ denotes the usual inner product in $L^2(\Omega)$ and $\|.\|$ represents the corresponding norm. We assume the following conditions:

$H_1 : D_T \in C_b^1(\mathbb{R})$ and $D_T \geq \beta_0 > 0$ in $\mathbb{R}$,
$H_2 : |G(T)| \leq \beta_1 |T|$ in $\mathbb{R}$,
$H_3 : |v(T)| \leq \beta_2 |T|$ in $\mathbb{R}$,
$H_4 : D_d \in C_b^1(\mathbb{R})$ and $D_d \geq \beta_3 > 0$ in $\mathbb{R}$,
$H_5 : |Q(c)| \leq \beta_4 |c|$ in $\mathbb{R}$,

where $C_b^1(\mathbb{R})$ denotes the space of bounded functions with bounded derivative in $\mathbb{R}$. To obtain upper bounds for the temperature and concentration, the previous assumptions will be used. To establish the stability of the weak problem (8), (9), H_2, H_3 and H_5 will be replaced by

$H_2^* : G \in C_b^1(\mathbb{R})$,
$H_3^* : v \in C_b^1(\mathbb{R})$,
$H_5^* : Q \in C_b^1(\mathbb{R})$,

respectively.

1.*Energy estimates for the solution of (8), (9)*:

The study of existence of solution for the coupled system (8) and (9) is not addressed in this paper. We present energy estimates for the solution of the system and for the corresponding fully discretized problem.

Energy estimate for the temperature: Taking in (8) $u = T(t)$, we get

$$\frac{1}{2}\frac{d}{dt}\|T(t)\|^2 + \beta_0\|\nabla T(t)\|^2 \leq \beta_1\|T(t)\|^2.$$

This inequality leads to

$$\|T(t)\|^2 + 2\beta_0\int_0^t \|\nabla T(s)\|^2 ds \leq \|T(0)\|^2 + 2\beta_1\int_0^t \|T(s)\|^2 ds. \tag{10}$$

If $T \in C^1([0,T_f], L^2(\Omega)) \cap L^2(0,T_f,H_0^1(\Omega))$, by the Gronwall Lemma we conclude

$$\|T(t)\|^2 + \int_0^t \|\nabla T(s)\|^2 ds \leq \frac{1}{\min\{1,2\beta_0\}} e^{2\beta_1 t}\|T(0)\|^2,\ t \in [0,T_f]. \tag{11}$$

Energy estimate for the concentration: Let $w = c(t)$ in (9). As $H_0^1(\Omega)$ is continuously embedded in $C^0(\overline{\Omega})$, we have successively

$$\begin{aligned} |(v(T)c(t), \nabla c(t))| &\leq \beta_2\|T(t)\|_\infty\|c(t)\|\|\nabla c(t)\| \\ &\leq \tfrac{1}{4\epsilon_1^2}\beta_2^2\|T(t)\|_\infty^2\|c(t)\|^2 + \epsilon_1^2\|\nabla c(t)\|^2, \end{aligned} \tag{12}$$

where $\epsilon_1 \neq 0$ is an arbitrary constant. Then, from (9) and (12), we easily get

$$\begin{aligned} &\|c(t)\|^2 + 2(\beta_3 - \epsilon_1^2)\int_0^t \|\nabla c(s)\|^2 ds \\ &\quad\leq \|c(0)\|^2 + \int_0^t \Big(\frac{1}{2\epsilon_1^2}\beta_2^2\|T(s)\|_\infty^2 + 2\beta_4\Big)\|c(s)\|^2 ds. \end{aligned} \tag{13}$$

If $T \in C([0,T_f], H_0^1(\Omega))$ then, for ϵ_1 such that $\beta_3 - \epsilon_1^2 > 0$, we guarantee the existence of two positive constants $\gamma_{c,i}, i = 1,2$, such that

$$\|c(t)\|^2 + \int_0^t \|\nabla c(s)\|^2 ds \leq \gamma_{c,1}\|c(0)\|^2 e^{\gamma_{c,2}\int_0^t \left(\|T(s)\|_\infty^2 + 1\right) ds},\ t \in [0,T_f], \tag{14}$$

provided that $c \in C^1([0,T_f], L^2(\Omega)) \cap L^2(0,T_f,H_0^1(\Omega))$.

As $\|T(t)\|_\infty \leq \|\nabla T(t)\|$, instead of (14), we have

$$\|c(t)\|^2 + \int_0^t \|\nabla c(s)\|^2 ds \leq \gamma_{c,1}\|c(0)\|^2 e^{\gamma_{c,2}\int_0^t \left(\|\nabla T(s)\|^2 + 1\right) ds},\ t \in [0,T_f]. \tag{15}$$

The term $\displaystyle\int_0^t \|\nabla T(s)\|^2 ds$ in (11) is bounded, for $t \in [0,T_f]$.

As

$$|(v(T)c(t), \nabla c(t))| \leq \beta_2\|T(t)\|\|\nabla c(t)\|^2, \tag{16}$$

if the drug convection-diffusion equation (4) is diffusion dominated in the sense that

$$\beta_3 - \beta_2\|T(t)\| > \gamma_{c,c} > 0 \text{ a.e. in } (0, T_f), \tag{17}$$

then c satisfies

$$\|c(t)\|^2 + 2\gamma_{c,c}\int_0^t \|\nabla c(s)\|^2 ds \leq \|c(0)\|^2 e^{2\beta_4 t}, t \in [0, T_f]. \tag{18}$$

Moreover, if the reaction term Q satisfies

H_5' : $Q \in C^1(\mathbb{R})$, and $Q(0) = 0$, $Q'(c) \leq \beta_4 \leq 0$ in $\mathbb{R}$,

instead of H_5, then (18) holds, and it can also be proved that

$$\|c(t)\|^2 + 2\gamma_{c,c}\int_0^t e^{2\beta_4(t-s)}\|\nabla c(s)\|^2 ds \leq \|c(0)\|^2 e^{2\beta_4 t}, t \in [0, T_f]. \tag{19}$$

2.*Stability estimates*:

Let $T, \tilde{T}$ and $c, \tilde{c}$ be solutions with initial conditions $c_0, \tilde{c}_0$ and $T_0, \tilde{T}_0$, respectively. Under the assumptions specified before, for $T, \tilde{T}$ and $c, \tilde{c}$ hold the energy estimates previously established. In what follows we will obtain estimates for $T - \tilde{T}$ and $c - \tilde{c}$.

For the temperature: Considering that T and $\tilde{T}$ satisfy (8), for $\omega_T(t) = T - \tilde{T}$ we obtain

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|\omega_T(t)\|^2 \quad &+((D_T(T) - D_T(\tilde{T}))\nabla T, \nabla\omega_T(t)) + (D_T(\tilde{T})\nabla\omega_T(t), \nabla\omega_T(t)) \\ &= (G(T) - G(\tilde{T}), \omega_T(t)).\end{aligned}$$

Using the assumption H_1, we have, successively,

$$\begin{aligned}&|((D_T(T) - D_T(\tilde{T}))\nabla T, \nabla\omega_T(t))| \\ &\quad\leq \|D_T'\|_{L^\infty(\mathbb{R})}\|\omega_T(t)\|\|\nabla T(t)\|_{L^\infty}\|\nabla\omega_T(t)\| \\ &\quad\leq \frac{1}{4\epsilon_1^2}\|D_T'\|^2_{L^\infty(\mathbb{R})}\|\nabla T(t)\|^2_{L^\infty}\|\omega_T(t)\| + \epsilon_1^2\|\nabla\omega_T(t)\|^2,\end{aligned} \tag{20}$$

where $\epsilon_1 \neq 0$. Using now H_2^*, we obtain

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|\omega_T(t)\|^2 \quad &+(\beta_0 - \epsilon_1^2)\|\nabla\omega_T(t)\|^2 \\ &\leq \Big(G'_{max} + \frac{1}{4\epsilon_1^2}\|D_T'\|^2_{L^\infty(\mathbb{R})}\|\nabla T(t)\|^2_{L^\infty}\Big)\|\omega_T(t)\|^2,\end{aligned} \tag{21}$$

If $\beta_0-\epsilon_1^2>0$ and $T,\tilde{T}\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega)\cap W^{1,\infty}(\Omega))$, from (21) we obtain

$$\begin{aligned}\|\omega_T(t)\|^2 &+2(\beta_0-\epsilon_1^2)\int_0^t\|\nabla\omega_T(s)\|^2ds\\ &\leq \|\omega_T(0)\|^2+\int_0^t\Big(2G'_{max}+\frac{1}{2\epsilon_1^2}\|D'_T\|^2_{L^\infty(\mathbb{R})}\|\nabla T(s)\|^2_{L^\infty}\Big)\|\omega_T(s)\|^2ds.\end{aligned}$$

that leads to

$$\begin{aligned}\|\omega_T(t)\|^2 &+2(\beta_0-\epsilon_1^2)\int_0^t e^{\int_s^t\left(2G'_{max}+\frac{1}{2\epsilon_1^2}\|D'_T\|^2_{L^\infty(\mathbb{R})}\|\nabla T(\mu)\|^2_{L^\infty}\right)d\mu}\|\nabla\omega_T(s)\|^2ds\\ &\leq \|\omega_T(0)\|^2e^{\int_0^t\left(2G'_{max}+\frac{1}{2\epsilon_1^2}\|D'_T\|^2_{L^\infty(\mathbb{R})}\|\nabla T(s)\|^2_{L^\infty}\right)ds},t\in[0,T_f].\end{aligned} \tag{22}$$

From (22) the stability is concluded for $T\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega)\cap W^{1,\infty}(\Omega))$ and $\tilde{T}\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega))$.

The smoothness of T can be weakened if we impose a stronger condition on $\|\nabla T(t)\|$. In fact, instead of (20), we can easily deduce

$$\begin{aligned}&|((D_T(T)-D_T(\tilde{T}))\nabla T,\nabla\omega_T(t))|\\ &\quad\leq \|D'_T\|_{L^\infty(\mathbb{R})}\|\nabla T(t)\|\|\nabla\omega_T(t)\|^2.\end{aligned}$$

If

$$\beta_0-\|D'_T\|_{L^\infty(\mathbb{R})}\|\nabla T(t)\|\geq\gamma_T>0 \text{ a.e.}\quad \text{in}\,(0,T_f), \tag{23}$$

for some positive constant γ_T, instead of (22), we conclude

$$\begin{aligned}\|\omega_T(t)\|^2 &+2\gamma_T\int_0^t e^{2G'_{max}(t-s)}\|\nabla\omega_T(s)\|^2ds\\ &\leq\|\omega_T(0)\|^2e^{2G'_{max}t},t\in[0,T_f].\end{aligned} \tag{24}$$

The stability inequality (24) allows us to conclude the stability for $T,\tilde{T}\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega))$ provided that T satisfies (23).

For the concentration: For the convection term we have

$$
\begin{aligned}
&|(v(T)c(t) - v(\tilde{T})\tilde{c}(t), \nabla\omega_c(t))| \\
&\quad = |((v(T) - v(\tilde{T}))c(t) + v(\tilde{T})\omega_c(t), \nabla\omega_c(t))| \\
&\quad \leq \|v'\|_{L^\infty(\mathbb{R})}\|\omega_T(t)\|_{L^2}\|c(t)\|_{L^\infty}\|\nabla\omega_c(t)\| + \beta_2\|\tilde{T}(t)\|_{L^\infty}\|\omega_c(t)\|\|\nabla\omega_c(t)\| \\
&\quad \leq \frac{1}{4\epsilon_1^2}\|v'\|^2_{L^\infty(\mathbb{R})}\|c(t)\|^2_{L^\infty}\|\omega_T(t)\|^2 + \frac{1}{4\epsilon_2^2}\beta_2^2\|\tilde{T}(t)\|^2_{L^\infty}\|\omega_c(t)\|^2 \\
&\quad +(\epsilon_1^2 + \epsilon_2^2)\|\nabla\omega_c(t)\|^2,
\end{aligned}
\tag{25}
$$

with $\epsilon_i \neq 0, i = 1, 2$, arbitrary constants.
For the diffusion term we get

$$
\begin{aligned}
&(D_d(T)\nabla c(t) - D_d(\tilde{T})\nabla\tilde{c}(t), \nabla\omega_c(t)) \\
&\quad = ((D_d(T) - D_d(\tilde{T}))\nabla c(t) + D_d(\tilde{T})\nabla\omega_c(t), \nabla\omega_c(t)),
\end{aligned}
$$

where

$$
\begin{aligned}
&|((D_d(T) - D_d(\tilde{T}))\nabla c(t), \nabla\omega_c(t))| \\
&\quad \leq \|D_d'\|_{L^\infty(\mathbb{R})}\|\omega_T(t)\|\|\nabla c(t)\|_{L^\infty}\|\nabla\omega_c(t)\| \\
&\quad \leq \tfrac{1}{4\epsilon_3^2}\|D_d'\|^2_{L^\infty(\mathbb{R})}\|\nabla c(t)\|^2_{L^\infty}\|\omega_T(t)\|^2 + \epsilon_3^2\|\nabla\omega_c(t)\|^2
\end{aligned}
\tag{26}
$$

and

$$
(D_d(\tilde{T})\nabla\omega_c(t), \nabla\omega_c(t)) \geq \beta_3\|\nabla\omega_c(t)\|^2.
$$

Then we obtain the differential inequality

$$
\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\|\omega_c(t)\|^2 + (\beta_3 - \epsilon_1^2 - \epsilon_2^2 - \epsilon_3^2)\|\nabla\omega_c(t)\|^2 \\
&\quad \leq \Big(\frac{\beta_2^2}{4\epsilon_2^2}\|\nabla\tilde{T}(t)\|^2 + Q'_{max}\Big)\|\omega_c(t)\|^2 \\
&\quad +\Big(\frac{1}{4\epsilon_1^2}\|v'\|^2_{L^\infty(\mathbb{R})}\|c(t)\|^2_{L^\infty} + \frac{1}{4\epsilon_3^2}\|D_d'\|^2_{L^\infty(\mathbb{R})}\|\nabla c(t)\|^2_{L^\infty}\Big)\|\omega_T(t)\|^2
\end{aligned}
\tag{27}
$$

whose solution satisfies

$$\begin{aligned}
&\|\omega_c(t)\|^2 + 2(\beta_3 - \epsilon_1^2 - \epsilon_2^2 - \epsilon_3^2)\int_0^t e^{\int_s^t \left(\frac{\beta_2^2}{2\epsilon_2^2}\|\nabla \tilde{T}(\mu)\|^2 + 2Q'_{max}\right)d\mu}\|\nabla\omega_c(s)\|^2 ds\\
&\le \|\omega_c(0)\|^2 e^{\int_0^t \left(\frac{\beta_2^2}{2\epsilon_2^2}\|\nabla \tilde{T}(\mu)\|^2 + 2Q'_{max}\right)d\mu}\\
&+ \int_0^t e^{\int_s^t \left(\frac{\beta_2^2}{2\epsilon_2^2}\|\nabla \tilde{T}(\mu)\|^2 + 2Q'_{max}\right)d\mu}\\
&\Big(\frac{1}{2\epsilon_1^2}\|v'\|^2_{L^\infty(\mathbb{R})}\|c(s)\|^2_{L^\infty} + \frac{1}{2\epsilon_3^2}\|D'_d\|^2_{L^\infty(\mathbb{R})}\|\nabla c(s)\|^2_{L^\infty}\Big)\|\omega_T(s)\|^2 ds,
\end{aligned} \tag{28}$$

for $t \in [0, T_f]$ and provided that $c \in C^1([0,T_f], L^2(\Omega)) \cap L^2(0, T_f, H^1_0(\Omega) \cap W^{1,\infty}(\Omega))$, $\tilde{c} \in C^1([0,T_f], L^2(\Omega)) \cap L^2(0,T_f,H^1_0(\Omega))$, $T \in L^2(0,T_f,L^2(\Omega))$, $\tilde{T} \in L^2(0,T_f,H^1_0(\Omega))$.

Finally for $\epsilon_i, i = 1,2,3$, such that $\beta_3 - \sum_{i=1}^{3}\epsilon_i^2 > 0$, we get the desired upper bound.

To conclude we recall that an upper bound for $\int_0^t \|\nabla\tilde{T}(\mu)\|^2 d\mu$ is established in (11) and upper bounds for $\|\omega_T(t)\|^2_{L^2}$ are defined in (22) or (24) when $\tilde{T} \in C^1([0,T_f], L^2(\Omega)) \cap L^2(0,T,H^1_0(\Omega))$ and $T \in C^1([0,T_f], L^2(\Omega)) \cap L^2(0,T,H^1_0(\Omega)\cap W^{1,\infty}(\Omega))$.
From (28), the stability of (8) and (9) is concluded when $c \in L^\infty(0,T_f,H^1_0(\Omega)\cap W^{1,\infty}(\Omega)) \cap C^1([0,T_f],L^2(\Omega))$, $T \in C^1([0,T_f],L^2(\Omega)) \cap L^2(0,T_f,H^1_0(\Omega))$ and for $\tilde{c}, \tilde{T} \in C^1([0,T_f],L^2(\Omega)) \cap L^2(0,T_f,H^1_0(\Omega))$.

In what follows we obtain more precise stability estimates under weaker assumptions. As $\|\omega_T(t)\|_\infty \le \|\nabla\omega_T(t)\|$, (25) and (26) are replaced by

$$\begin{aligned}
&|(v(T)c(t) - v(\tilde{T})\tilde{c}(t), \nabla\omega_c(t))|\\
&\quad \le \Big(\frac{1}{4\epsilon_1^2}\|v'\|^2_{L^\infty(\mathbb{R})}\|c(t)\|^2\|\nabla\omega_T\|^2 + \frac{1}{4\epsilon_2^2}\beta_2^2\|\nabla\tilde{T}(t)\|^2\|\omega_c(t)\|^2\\
&\quad +(\epsilon_1^2+\epsilon_2^2)\|\nabla\omega_c(t)\|^2
\end{aligned}$$

and

$$\begin{aligned}
&|((D_d(T) - D_d(\tilde{T}))\nabla c(t), \nabla\omega_c(t))|\\
&\quad \le \tfrac{1}{4\epsilon_3^2}\|D'_d\|^2_{L^\infty(\mathbb{R})}\|\nabla c(t)\|^2\|\nabla\omega_T(t)\|^2 + \epsilon_3^2\|\nabla\omega_c(t)\|^2,
\end{aligned}$$

respectively.

Consequently, (28) is replaced by

$$\begin{aligned}
&\|\omega_c(t)\|^2 + 2(\beta_3 - \sum_{i=1}^{3}\epsilon_i^2)\int_0^t e^{\int_s^t\left(\frac{\beta_2^2}{2\epsilon_2^2}\|\nabla\tilde{T}(\mu)\|^2+2Q'_{max}\right)d\mu}\|\nabla\omega_c(s)\|^2 ds\\
&\quad\le \|\omega_c(0)\|^2 e^{\int_0^t\left(\frac{\beta_2^2}{2\epsilon_2^2}\|\nabla\tilde{T}(\mu)\|^2+2Q'_{max}\right)d\mu}\\
&\quad+\int_0^t e^{\int_s^t\left(\frac{\beta_2^2}{2\epsilon_2^2}\|\nabla\tilde{T}(\mu)\|^2+2Q'_{max}\right)d\mu}\Big(\frac{1}{2\epsilon_1^2}\|v'\|^2_{L^\infty(\mathbb{R})}\|c(s)\|^2\\
&\quad+\frac{1}{2\epsilon_3^2}\|D'_d\|^2_{L^\infty(\mathbb{R})}\|\nabla c(s)\|^2\Big)\|\nabla\omega_T(s)\|^2 ds\Big),\ t\in[0,T_f].
\end{aligned} \tag{29}$$

An upper bound for $\int_0^t \|\nabla\tilde{T}(\mu)\|^2 d\mu$ is given by (11). Upper bounds for $\int_0^t \|\nabla\omega_T(s)\|^2 ds$ are defined by (22) provided that $T\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega)\cap W^{1,\infty}(\Omega))$ and for $\tilde{T}\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega))$; or by (24) provided that (23) holds and $T,\tilde{T}\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega))$. From (29) we conclude the stability of the initial value problem (8) and (9) for $c\in L^\infty(0,T_f,H_0^1(\Omega))\cap C^1([0,T_f],L^2(\Omega))$, $T\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T,H_0^1(\Omega))$ and for $\tilde{c},\tilde{T}\in C^1([0,T_f],L^2(\Omega))\cap L^2(0,T_f,H_0^1(\Omega))$.

3. A FEM that mimics the continuous model: stability analysis

3.1. Fully discrete FEM. In this section we present a fully discrete method that mimics system (8) and (9).

Let $h=(h_1,\dots,h_N)$ be a vector of positive entries such that $\sum_{i=1}^N h_i = 1$ and $h_{max}=\max_i h_i$. Let Λ be a sequence of vectors h defined as before and such that $h_{max}\to 0$. Let $\overline{\Omega}_h=\{x_i, i=0,\dots,N\}$ be the non-uniform grid in Ω induced by h, with $x_i-x_{i-1}=h_i, x_0=0, x_N=1$. By Ω_h and $\partial\Omega_h$ we denote the interior set of nodes $\Omega_h=\Omega\cap\overline{\Omega}_h$ and the boundary points $\partial\Omega_h=\partial\Omega\cap\overline{\Omega}_h$.

By W_h we represent the space of grid functions defined in $\overline{\Omega}_h$ and let $W_{h,0}=\{w_h\in W_h : w_h = 0 \,\text{on}\, \partial\Omega_h\}$. For $w_h\in W_h$, $P_h w_h$ denotes the continuous piecewise linear interpolation of w_h with respect to the partition $\overline{\Omega}_h$.

In $W_{h,0}$ we introduce the inner product

$$(u_h, w_h)_h = \sum_{i=1}^{N-1} h_{i+1/2} u_h(x_i) w_h(x_i),\ u_h, w_h \in W_{h,0},$$

where $h_{i+1/2} = \frac{1}{2}(h_i + h_{i+1})$. Let $\|.\|_h$ be the corresponding norm. We introduce $x_{i+1/2} = x_i + \dfrac{h_{i+1}}{2}$, $x_{i-1/2} = x_i - \dfrac{h_i}{2}$.

For $u_h, w_h \in W_h$, we use the notations

$$(u_h, w_h)_+ = \sum_{i=1}^{N} h_i u_h(x_i) w_h(x_i),$$

and

$$\|w_h\|_+ = \sqrt{(w_h, w_h)_+}.$$

Let D_{-x} be the usual backward finite difference operator. We recall that holds the following discrete Poincaré-Friedrichs inequality

$$\|w_h\|_h^2 \le \|D_{-x} w_h\|_+^2,\ \forall w_h \in W_{h,0}. \tag{30}$$

By $\|.\|_{1,h}$ we represent the norm $\|u_h\|_{1,h} = \left(\|u_h\|_h^2 + \|D_{-x} u_h\|_+^2\right)^{1/2}$. The piecewise linear finite element approximations for the solutions of (8) and (9) are defined as follow: $P_h T_h(t), P_h c_h(t) \in H_0^1(\Omega)$ such that

$$\begin{aligned}(P_h T_h'(t), P_h u_h) &= -(D_T(P_h T_h(t)) \nabla P_h T_h(t), \nabla P_h u_h) \\ &\quad + (G(P_h T_h), P_h u_h), \forall u_h \in W_{h,0},\end{aligned} \tag{31}$$

and

$$\begin{aligned}(P_h c_h'(t), P_h w_h) &\ -(v(P_h T_h) P_h c_h(t), \nabla P_h w_h) \\ &= -(D_d(P_h T_h(t)) \nabla P_h c_h(t), \nabla P_h w_h) \\ &\quad + (Q(P_h c_h(t)), P_h w_h), \forall w_h \in W_{h,0}.\end{aligned} \tag{32}$$

To define the fully discrete piecewise linear approximations for the temperature and concentration we need to define the approximations for the integrals terms in (31) and (32).

Considering the approximations rules defined before by one of the authors in [7], we introduce the following approximations:

$$(f, g) \simeq (R_h f, R_h g),\ f, g \in C(\overline{\Omega}), \tag{33}$$

where R_h denotes the restriction operator,

$$(a(P_hq_h)\nabla P_hu_h, \nabla P_hw_h) \simeq (a(M_hq_h)D_{-x}u_h, D_{-x}w_h)_+, q_h, u_h, w_h \in W_{h,0}, \tag{34}$$

where M_h is the average operator

$$M_hq_h(x_i) = \frac{1}{2}(q_h(x_{i-1}) + q_h(x_i)), i = 1, \ldots, N.$$

Taking into account the previous approximation rule, the variational problem for the finite element approximation $P_hT_h(t)$ is placed by the following fully discrete FEM: compute $T_h(t) \in W_{h,0}$ such that

$$\begin{array}{ll}(T_h'(t), u_h)_h & = -(D_T(M_hT_h(t))D_{-x}T_h(t), D_{-x}u_h)_+ \\ & +(G(T_h(t)), u_h)_h, \forall u_h \in W_{h,0}.\end{array} \tag{35}$$

To define the fully discrete problem for the concentration, we need to introduce the approximation of the integral term associated with the convective term $(v(P_hT_h)P_hc_h(t), \nabla P_hw_h)$. We consider

$$(v(P_hT_h)P_hc_h(t), \nabla P_hw_h) \simeq (M_h(v(T_h)c_h), D_{-x}w_h)_+.$$

Using the introduced quadrature rules in (32), we get the fully discrete FEM: compute $c_h(t) \in W_{h,0}$ such that

$$\begin{array}{ll}(c_h'(t), w_h)_h & -(M_h(v(T_h(t))c_h(t)), D_{-x}w_h)_+ \\ & = -(D_d(M_hT_h(t))D_{-x}c_h(t), D_{-x}w_h)_+ \\ & +(Q(c_h(t)), w_h)_h, \forall w_h \in W_{h,0}.\end{array} \tag{36}$$

We remark that the coupled system (35), (36) can be rewritten as a ordinary differential systems. To do that, we need to introduce the difference quotient $D_x^*(a(M_hq_h)D_{-x}u_h)$ defined by

$$\begin{array}{ll}D_x^*(a(M_hq_h)D_{-x}u_h)(x_i) & = \frac{1}{h_{i+1/2}}\Big(a(M_hq_h(x_{i+1}))D_{-x}u_h(x_{i+1}) \\ & -a(M_hq_h(x_i))D_{-x}u_h(x_i)\Big),\end{array}$$

for $i = 1, \ldots, N-1$, and for $q_h, u_h \in W_{h,0}$, and the first order centered finite difference operator

$$D_c(u_h)(x_i) = \frac{u_h(x_{i+1}) - u_h(x_{i-1})}{h_i + h_{i+1}}, i = 1, \ldots, N-1.$$

We introduce now the ordinary differential systems

$$\begin{cases} T_h'(t) = F_T(T_h(t)) \text{ in}\, \Omega_h \times (0, T_f] \\ T_h(t) = 0 \,\text{in}\, \partial\Omega_h \times (0, T_f] \\ T_h(0) = R_h T_0 \text{in}\, \Omega_h, \end{cases} \tag{37}$$

and

$$\begin{cases} c_h'(t) = F_c(T_h(t), c_h(t)) \text{ in}\, \Omega_h \times (0, T_f] \\ c_h(t) = 0 \,\text{in}\, \partial\Omega_h \times (0, T_f] \\ c_h(0) = R_h c_0 \text{in}\, \Omega_h, \end{cases} \tag{38}$$

where the following notations were used

$$F_T(T_h(t)) = D_x^*(D_T(M_h T_h(t)) D_{-x} T_h(t)) + G(T_h(t))$$

and

$$F_c(T_h(t), c_h(t)) = D_x^*(D_d(M_h T_h(t)) D_{-x} c_h(t)) - D_c(v(T_h(t)) c_h(t)) + Q(c_h(t)).$$

Considering the inner product of the first equation of (37) and (38), with respect to $(.,.)_h$, by $u_h \in W_{h,0}$ and $w_h \in W_{h,0}$, respectively, we get (35) and (36). This results shows the equivalence between the fully discrete FEM (35), (36) and the FDMs (37) and (38), respectively.

3.2. Stability. We start this section establishing energy upper bounds for $\|T_h(t)\|_h$ and $\|c_h(t)\|_h$ analogous of the ones established before for the continuous counterpart.

Firstly we establish the existence of the semi-discrete approximations, at least locally, this means that there exists an interval $[0, T_f]$ and functions $T_h(t), c_h(t)$ solutions of the ordinary differential problems (37) and (38).

We observe that the previous coupled problem can be rewritten in the following equivalent form

$$\begin{cases} Z_h'(t) = F_h(Z_h(t)) \,\text{in}\, \Omega_h \times (0, T_f], \\ Z_h(0) = Z_{0,h} \,\text{in}\, \Omega_h, \\ Z_h(t) = 0 \,\text{in}\, \partial\Omega_h \times (0, T_f], \end{cases} \tag{39}$$

where $Z_h(t) = (T_h(t), c_h(t)), Z_{0,h} = (R_h T_0, R_h c_0)$ and

$$F_h(Z_h(t)) = (F_T(T_h(t)), F_c(T_h(t), c_h(t))).$$

Proposition 1. *Under the assumptions* H_1, H_2^*, H_3^*, H_4 *and* H_5^*,

$$F_h : B_{\delta_T}(R_h T_0) \times B_{\delta_c}(R_h c_0) \to [W_{h,0}]^2$$

is one-side Lipschitz, where

$$B_\delta(u_h) = \{z_h \in W_{h,0} : \|z_h - u_h\|_h \leq \delta\},$$

for $u_h = R_h T_0, R_h c_0$, *and* $\delta = \delta_T, \delta_c$.

Proof: Let $Z_h = (q_h, w_h), \tilde{Z}_h = (\tilde{q}_h, \tilde{w}_h) \in B_{\delta_T}(R_h T_0) \times B_{\delta_c}(R_h c_0)$, and $\omega_q = q_h - \tilde{q}_h$, $\omega_w = w_h - \tilde{w}_h$ and $\omega = (\omega_q, \omega_w)$. We have, successively, the following

$$\begin{aligned}(F_h(Z_h) - F_h(\tilde{Z}_h), \omega)_{[W_{h,0}]^2} &= (F_T(q_h) - F_T(\tilde{q}_h), \omega_q)_h \\ &+(F_c(q_h, w_h) - F_c(\tilde{q}_h, \tilde{w}_h), \omega_w)_h,\end{aligned}$$

$$\begin{aligned}(F_T(q_h) &-F_T(\tilde{q}_h), \omega_q)_h = -((D_T(M_h q_h) - D_T(M_h \tilde{q}_h))D_{-x}q_h, D_{-x}\omega_q)_+ \\ &-(D_T(M_h\tilde{q}_h(t))D_{-x}\omega_q, D_{-x}\omega_q)_+ \\ &+(G(q_h) - G(\tilde{q}_h), \omega_q)_h \\ &\leq \sqrt{2}|D'_T|_{max}\|\omega_q\|_h\|D_{-x}q_h\|_\infty\|D_{-x}\omega_q\|_+ - \beta_0\|D_{-x}\omega_q\|_+^2 + G'_{max}\|\omega_q\|_h^2 \\ &\leq \Big(\frac{4}{\epsilon^2}\frac{1}{h_{min}^2}\Big(\delta_T + \|R_h T_0\|_h\Big)^2(D'_T)^2_{max} + G'_{max}\Big)\|\omega_q\|_h^2 \\ &+(-\beta_0 + \epsilon^2)\|D_{-x}\omega_q\|_+^2.\end{aligned}$$

Then, for $\epsilon^2 = \beta_0$, we obtain

$$\begin{aligned}(F_T(q_h) - F_T(\tilde{q}_h), \omega_q)_h &\leq \Big(\frac{4}{\beta_0}\frac{1}{h_{min}^2}\Big(\delta_T + \|R_h T_0\|_h\Big)^2(D'_T)^2_{max} + G'_{max}\Big)\|\omega_q\|_h^2 \\ &:= L_T(h)\|\omega_q\|_h^2.\end{aligned} \tag{40}$$

For $(F_c(q_h, w_h) - F_c(\tilde{q}_h, \tilde{w}_h), \omega_w)_h$ we establish

$$\begin{aligned}(F_c(q_h, w_h) &-F_c(\tilde{q}_h, \tilde{w}_h), \omega_w)_h = -((D_d(M_h q_h) - D_d(M_h\tilde{q}_h))D_{-x}w_h, D_{-x}\omega_w)_+ \\ &-D_d(M_h\tilde{q}_h))D_{-x}\omega_w, D_{-x}\omega_w)_+ \\ &+(M_h((v(q_h) - v(\tilde{q}_h))w_h, D_{-x}\omega_w)_+ \\ &+(M_h(v(\tilde{q}_h))\omega_w, D_{-x}\omega_w)_+ + Q'_{max}\|\omega_w\|_h^2 \\ &\leq \sqrt{2}|D'_d|_{max}\|\omega_q\|_h\|D_{-x}w_h\|_\infty\|D_{-x}\omega_w\|_+ \\ &-\beta_3\|D_{-x}\omega_w\|_+^2 + \sqrt{2}|v'|_{max}\|\omega_q\|_h\|w_h\|_\infty\|D_{-x}\omega_w\|_+ \\ &+\sqrt{2}\beta_2\|\tilde{q}_h\|_\infty\|\omega_w\|_h\|D_{-x}\omega_w\|_+ + Q'_{max}\|\omega_w\|_h^2 \\ &\leq \frac{1}{\epsilon^2}\Big(\frac{4}{h_{min}^2}(D'_d)^2_{max} + \frac{2}{h_{min}}(v')^2_{max}\Big) \\ &\Big(\delta_c + \|R_h c_0\|_h\Big)^2\|\omega_q\|_h^2 \\ &+\Big(\frac{\beta_2^2}{\epsilon^2}\frac{2}{h_{min}}\Big(\delta_T + \|R_h T_0\|_h\Big)^2 + Q'_{max}\Big)\|\omega_w\|_h^2 \\ &+(3\epsilon^2 - \beta_3)\|D_{-x}\omega_w\|_+^2.\end{aligned}$$

Choosing $\epsilon^2 = \frac{1}{3}\beta_3$, we conclude that

$$\begin{aligned}(F_c(q_h, w_h) \; & -F_c(\tilde{q}_h, \tilde{w}_h), \omega_w)_h \leq \frac{3}{\beta_3}\Big(\frac{4}{h_{min}}(D'_d)^2_{max} + \frac{2}{h_{min}}(v')^2_{max}\Big) \\ & \Big(\delta_c + \|R_h c_0\|_h\Big)^2 \|\omega_q\|_h^2 \\ & +\Big(\frac{6\beta_2^2}{\beta_3}\frac{1}{h_{min}}\Big(\delta_T + \|R_h T_0\|_h\Big)^2 + Q'_{max}\Big)\|\omega_w\|_h^2 \\ & := L_{c,1}(h)\|\omega_q\|_h^2 + L_{c,2}(h)\|\omega_w\|_h^2.\end{aligned} \tag{41}$$

From (40) and (41) we finally obtain

$$\begin{aligned}(F_h(Z_h) \; & -F_h(\tilde{Z}_h), Z_h - \tilde{Z}_h)_{[W_{h,0}]^2} \leq (L_T(h) + L_{c,1}(h))\|\omega_q\|_h^2 + L_{c,2}(h)\|\omega_w\|_h^2 \\ & \leq \max\{L_T(h) + L_{c,1}(h), L_{c,2}(h)\}\|Z_h - \tilde{Z}_h\|^2_{[W_{h,0}]^2}.\end{aligned} \tag{42}$$

■

We remark that the one-side Lipschitz condition (42), established in Proposition 1, guarantees the existence of the semi-discrete approximations $T_h(t), c_h(t)$, at least locally.

We observe that if we use the previous result to get upper bounds for $\|\omega_h(t)\|_{[W_{h,0}]^2}$, where $\omega_h(t) = Z_h(t) - \tilde{Z}_h(t)$, $Z_h(t) = (T_h(t), c_h(t))$ is the solution of (39) with initial condition $Z_h(0)$, and $\tilde{Z}_h(t)$ is the solution of the same problem but with perturbed initial condition $\tilde{Z}_h(0)$, then we have

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|\omega_h(t)\|^2_{[W_{h,0}]^2} & = (F_h(Z_h(t)) - F_h(\tilde{Z}_h(t)), \omega_h(t))_{[W_{h,0}]^2} \\ & \leq \max\{L_T(h) + L_{c,1}(h), L_{c,2}(h)\}\|\omega_h(t)\|^2_{[W_{h,0}]^2},\end{aligned} \tag{43}$$

where $L_T(h), L_{c,1}(h)$ and $L_{c,2}(h)$ are defined in Proposition 1. Consequently, we obtain

$$\|\omega_h(t)\|^2_{[W_{h,0}]^2} \leq e^{2\max\{L_T(h)+L_{c,1}(h), L_{c,2}(h)\}t}\|\omega_h(0)\|^2_{[W_{h,0}]^2}, t \geq 0. \tag{44}$$

The upper bound (44) guarantees the stability of the semi-discretization defined by F_h in bounded time intervals for each h. However, when h decreases, from this upper bound we are not able to conclude such stability behaviour. This fact is our motivation to study the stability using the energy method for each semi-discretization defined by F_T and F_c. To obtain the stability upper bounds, we start by establishing convenient upper bounds for $T_h(t)$ and $c_h(t)$ which are solutions of (35) and (36), respectively.

1.*Energy estimates*:

For the temperature $T_h(t)$: Taking in (35) $u_h = T_h(t)$, and following the steps used to prove (11), we easily get

$$\|T_h(t)\|_h^2 + \int_0^t \|D_{-x}T_h(s)\|_+^2 ds \le \frac{1}{\min\{1, 2\beta_0\}} e^{2\beta_1 t}\|T_h(0)\|_h^2, \qquad (45)$$

for $t \in [0, T_f]$, provided that $T_h \in C^1([0, T_f], W_{h,0})$.

For the concentration: Let $w_h = c_h(t)$ in (36). As in the continuous case, we have

$$\begin{aligned} &|(M_h(v(T_h(t))c_h(t)), D_{-x}c_h(t))_+| \\ &\quad \le \sqrt{2}\beta_2\|T_h(t)\|_\infty\|c_h(t)\|_h\|D_{-x}c_h(t)\|_+ \\ &\quad \le \frac{1}{2\epsilon_1^2}\beta_2^2\|T_h(t)\|_\infty^2\|c_h(t)\|_h^2 + \epsilon_1^2\|D_{-x}c_h(t)\|_+^2, \end{aligned} \qquad (46)$$

where $\epsilon_1 \neq 0$ is an arbitrary constant. Then, for ϵ_1 such that $\beta_3 - \epsilon_1^2 > 0$, we easily get

$$\|c_h(t)\|_h^2 + \int_0^t \|D_{-x}c_h(s)\|_+^2 ds \le \frac{1}{\min\{1, 2(\beta_3 - \epsilon_1^2)\}}\|c_h(0)\|_h^2 e^{\int_0^t \left(\frac{\beta_2^2}{\epsilon_1^2}\|T_h(s)\|_\infty^2 + 2\beta_4\right) ds}, \qquad (47)$$

for $t \in [0, T_f]$, provided that $c_h \in C^1([0, T_f], W_{h,0})$.

From (45), the term $\int_0^t \|D_{-x}T_h(s)\|_+^2 ds$ is uniformly bounded in $[0, T_f]$, provided that $\|T_h(0)\|_h$ is uniformly bounded in $h \in \Lambda$. As $\int_0^t \|T_h(s)\|_\infty^2 ds \le \int_0^t \|D_{-x}T_h(s)\|_+^2 ds$, we have $\int_0^t \|T_h(s)\|_\infty^2 ds \le \frac{1}{\min\{1, 2\beta_0\}} e^{2\beta_1 t}\|T_h(0)\|_h^2$ and then

$$\|c_h(t)\|_h^2 + \int_0^t \|D_{-x}c_h(s)\|_+^2 ds \le \gamma_{c,1}\|c_h(0)\|_h^2 e^{\frac{\beta_2^2}{\epsilon_1^2}\frac{1}{\min\{1,2\beta_0\}}e^{2\beta_1 t}\|T_h(0)\|_h^2 + 2\beta_4 t}, t \in [0, T_f]. \qquad (48)$$

However, (46) can be replaced by

$$\begin{aligned} &|(M_h(v(T_h(t))c_h(t)), D_{-x}c_h(t))_+| \\ &\quad \le \sqrt{2}\beta_2\|T_h(t)\|_h\|c_h(t)\|_\infty\|D_{-x}c_h(t)\|_+ \\ &\quad \le \sqrt{2}\beta_2\|T_h(t)\|_h\|D_{-x}c_h(t)\|_+^2. \end{aligned} \qquad (49)$$

Then, if the discrete version of (17)

$$\epsilon_3 - \sqrt{2}\beta_2\|T_h(t)\|_h > \gamma_{c,c} > 0 \text{ a.e. in } (0, T_f),$$

holds, for some positive constant $\gamma_{c,c}$, then $c_h(t)$ satisfies the following discrete version of (18)

$$\|c_h(t)\|_h^2 + 2\gamma_{c,c}\int_0^t \|D_{-x}c_h(s)\|_+^2 ds \leq \|c_h(0)\|_h^2 e^{2\beta_4 t}, t \in [0, T_f]. \tag{50}$$

We remark that from (45), $\|T_h(t)\|_h$ is bounded in $[0, T_f]$.

2.*Stability estimates*:

In what follows we analyse the differences $\omega_T(t) = T_h(t) - \tilde{T}_h(t), \omega_c(t) = c(t) - \tilde{c}(t)$, when $T_h(t), \tilde{T}_h(t)$ and $c_h(t), \tilde{c}_h(t)$ are solutions of (36) and (35), respectively, with initial conditions $T_h(0), \tilde{T}_h(0)$ and $c_h(0), \tilde{c}_h(0)$, respectively.

For $\omega_T(t) = T_h(t) - \tilde{T}_h(t)$:

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|\omega_T(t)\|_h^2 \; & +((D_T(M_hT_h(t)) - D_T(M_h\tilde{T}_h(t)))D_{-x}T_h(t), D_{-x}\omega_T(t))_+ \\ & +(D_T(M_h\tilde{T}_h(t))D_{-x}\omega_T(t), D_{-x}\omega_T(t))_+ \\ & = (G(T_h(t)) - G(\tilde{T}_h(t)), \omega_T(t))_h.\end{aligned}$$

To establish an upper bound for

$$((D_T(M_hT_h(t)) - D_T(M_h\tilde{T}_h(t)))D_{-x}T_h(t), D_{-x}\omega_T(t))_+,$$

we need to impose an additional condition to $D_{-x}T_h(t)$

$$H_6 : \int_0^t \|D_{-x}T_h(t)\|_\infty^2 ds \text{ is uniformly bounded in } h \in \Lambda \text{ , } t \in (0, T_f).$$

Under the previous assumption we get

$$\begin{aligned} & ((D_T(M_hT_h(t)) - D_T(M_h\tilde{T}_h(t)))D_{-x}T_h(t), D_{-x}\omega_T(t))_+ \\ & \quad \leq \sqrt{2}(D_T')_{max}\|D_{-x}T_h(t)\|_\infty\|\omega_T(t)\|_h\|D_{-x}\omega_T(t)\|_+ \\ & \quad \leq \tfrac{1}{2\epsilon_1^2}(D_T')_{max}^2\|D_{-x}T_h(t)\|_\infty^2\|\omega_T(t)\|_h^2 + \epsilon_1^2\|D_{-x}\omega_T(t)\|_+^2. \end{aligned} \tag{51}$$

for $\epsilon_1 \neq 0$.

For ϵ_1 such that $\beta_0 - \epsilon_1^2 > 0$, it can be shown that

$$\begin{aligned}\|\omega_T(t)\|_h^2 \; & +2(\beta_0 - \epsilon_1^2)\int_0^t e^{\int_s^t \left(\frac{1}{2\epsilon_1^2}(D_T')_{max}^2\|D_{-x}T_h(\mu)\|_\infty^2 + 2G'_{max}\right)d\mu}\|D_{-x}\omega_T(s)\|_+^2 ds \\ & \leq \|\omega_T(0)\|_h^2 e^{\int_0^t \left(\frac{1}{2\epsilon_1^2}(D_T')_{max}^2\|D_{-x}T_h(s)\|_\infty^2 + 2G'_{max}\right)ds}, \; t \in [0, T_f].\end{aligned} \tag{52}$$

The assumption H_6 guarantees that the upper bound in (52) is bounded by $Const.\|\omega_T(0)\|_h$ in $[0, T_f]$. Consequently we conclude the stability of the FEM

(35), or equivalently, the stability of the FDM (37), in $T_h(t)$. We observe that it remains to analyse when H_6 effectively holds.

We can obtain another upper bound avoiding the assumption H_6. Observing that (51) can be replaced by replaced by

$$\begin{aligned}((D_T(M_hT_h(t)) - D_T(M_h\tilde{T}_h(t)))D_{-x}T_h(t), D_{-x}\omega_T(t))_+ \\ \leq |D'_T|_{max}\|D_{-x}T_h(t)\|_+\|\omega_T(t)\|_\infty\|D_{-x}\omega_T(t)\|_+ \\ \leq (D'_T)^2_{max}\|D_{-x}T_h(t)\|_+\|D_{-x}\omega_T(t)\|^2_+,\end{aligned} \tag{53}$$

we establish

$$\begin{aligned}\|\omega_T(t)\|^2_h \ &+2\gamma_T\int_0^t e^{2G'_{max}(t-s)}\|D_{-x}\omega_T(s)\|^2_+ ds \\ &\leq \|\omega_T(0)\|^2_h e^{2G'_{max}t},\ t\in[0,T_f],\end{aligned} \tag{54}$$

provided that

$$\beta_0 - (D'_T)^2_{max}\|D_{-x}T_h(t)\|_+ \geq \gamma_T > 0 \text{ a.e. in } (0,T_f), \tag{55}$$

for some positive constant γ_T.
From (53) we conclude the stability of (35) or equivalently (37) in $T_h(t)$ provided that (55) holds. Condition (55) means that $\|T_h(t)\|_{1,h}$ is a.e bounded in $(0,T_f)$ uniformly in $h\in\Lambda$.

For $\omega_c(t) = c_h(t) - \tilde{c}_h(t)$: For the convective term we deduce

$$\begin{aligned}&|(M_h\big(v(T_h)c_h(t) - v(\tilde{T}_h)\tilde{c}_h(t)\big), D_{-x}\omega_c(t))_+| \\ &\quad\leq \sqrt{2}|v'|_{max}\|\omega_T(t)\|_h\|c_h(t)\|_\infty\|D_{-x}\omega_c(t)\|_+ \\ &\quad+\sqrt{2}\beta_2\|\tilde{T}_h(t)\|_\infty\|\omega_c(t)\|_h\|D_{-x}\omega_c(t)\|_+ \\ &\quad\leq \frac{1}{2\epsilon_1^2}(v')^2_{max}\|\omega_T(t)\|^2_h\|c_h(t)\|^2_\infty + \frac{1}{2\epsilon_2^2}\beta_2^2\|\tilde{T}_h(t)\|^2_\infty\|\omega_c(t)\|^2_h \\ &\quad+(\epsilon_1^2+\epsilon_2^2)\|D_{-x}\omega_c(t)\|^2_+,\end{aligned} \tag{56}$$

with $\epsilon_i\neq 0, i=1,2,$ are arbitrary constants.

For the diffusion terms we get

$$\begin{aligned}&|((D_d(M_hT_h) - D_d(M_h\tilde{T}_h))D_{-x}c_h(t), D_{-x}\omega_c(t))_+| \\ &\quad\leq \sqrt{2}|D'_d|_{max}\|\omega_T(t)\|_h\|D_{-x}c_h(t)\|_\infty\|D_{-x}\omega_c(t)\|_+ \\ &\quad\leq \tfrac{1}{2\epsilon_3^2}(D'_d)^2_{max}\|\omega_T(t)\|^2_h\|D_{-x}c_h(t)\|^2_\infty + \epsilon_3^2\|D_{-x}\omega_c(t)\|^2_+\end{aligned} \tag{57}$$

and

$$(D_d(M_h\tilde{T}_h)D_{-x}\omega_c(t), D_{-x}\omega_c(t))_+ \geq \beta_3\|D_{-x}\omega_c(t)\|^2_+.$$

Following the steps used to establish (28) with the convenient adaptations, it can be show that, for $\epsilon_i \neq 0, i = 1, 2, 3$, such that $\beta_3 - \displaystyle\sum_{i=1}^{3} \epsilon_i^2 > 0$, we have

$$
\begin{aligned}
&\|\omega_c(t)\|_h^2 + \int_0^t e^{\int_s^t \left(\frac{\beta_2^2}{\epsilon_2^2}\|\tilde{T}_h(\mu)\|_\infty^2 + 2Q'_{max}\right)d\mu} \|D_{-x}\omega_c(s)\|_+^2 ds \\
&\quad \leq \frac{1}{\min\{1, 2(\beta_3 - \sum_{i=1}^{3}\epsilon_i^2)\}}\Big(\|\omega_c(0)\|_h^2 e^{\int_0^t \left(\frac{\beta_2^2}{\epsilon_2^2}\|\tilde{T}_h(s)\|_\infty^2 + 2Q'_{max}\right)ds} \\
&\quad + \int_0^t e^{\int_s^t \left(\frac{\beta_2^2}{\epsilon_2^2}\|\tilde{T}_h(\mu)\|_\infty^2 + 2Q'_{max}\right)d\mu} \Big(\frac{1}{\epsilon_1^2}(v')_{max}^2\|c_h(s)\|_\infty^2 + \frac{1}{\epsilon_3^2}(D'_d)_{max}^2\|D_{-x}c_h(s)\|_\infty^2\Big) \\
&\qquad\qquad \|\omega_T(s)\|_h^2 ds, \ t \in [0, T_f].
\end{aligned}
\tag{58}
$$

To conclude the stability of (35) and (36), we recall that an upper bound for $\|\omega_T(t)\|_h^2$ in $[0, T_f]$ is established in (52)(provided that H_6 holds) or (54) (provided that (55) holds) . To guarantee that the previous estimate holds, we need to assume that $T_h, \tilde{T}_h, c_h, \tilde{c}_h \in C^1([0, T_f], W_{h,0})$. However, the obtained upper bound will be h-dependent. To get a stability estimate h-independent, we need to assume that

$$
\int_0^t \|\tilde{T}_h(s)\|_\infty^2 ds \text{ and } \int_0^t \Big(\|c_h(s)\|_\infty^2 + \|D_{-x}c_h(s)\|_\infty^2\Big)\|\omega_T(s)\|_h^2 ds
$$

are uniformly bounded in $h \in \Lambda$. As $\displaystyle\int_0^t \|\tilde{T}_h(s)\|_\infty^2 ds \leq \int_0^t \|D_{-x}\tilde{T}_h(s)\|_+^2 ds$, then, by (45) or (47), $\displaystyle\int_0^t \|\tilde{T}_h(s)\|_\infty^2 ds$ is uniformly bounded in $h \in \Lambda$.

We observe now that an upper bound for $\|\omega_T(t)\|_h^2, t \in [0, T_f], h \in \Lambda$, is established in (52) or (54). Then to bound $\displaystyle\int_0^t \Big(\|c_h(s)\|_\infty^2 + \|D_{-x}c_h(s)\|_\infty^2\Big)\|\omega_T(s)\|_h^2 ds$, we need to guarantee that $\displaystyle\int_0^t \Big(\|c_h(s)\|_\infty^2 + \|D_{-x}c_h(s)\|_\infty^2\Big)ds$ is uniformly bounded in $h \in \Lambda$. As we will see later, to do that we assume an additional condition on the spatial grids $\Omega_h, h \in \Lambda$, and we show that $c_h(s)$ is a second order approximations for $c(t)$.

To get another upper bound for $\|\omega_c(t)\|_h$, we observe that the bounds (56) and (57) can be replaced, respectively, by

$$
\begin{aligned}
&|(M_h\big(v(T_h)c_h(t)-v(\tilde{T}_h)\tilde{c}_h(t)\big), D_{-x}\omega_c(t))_+| \\
&\quad\le \frac{1}{2\epsilon_1^2}(v')^2_{max}\|D_{-x}\omega_T(t)\|_+^2\|c_h(t)\|_h^2+\frac{1}{2\epsilon_2^2}\beta_2^2\|D_{-x}\tilde{T}_h(t)\|_+^2\|\omega_c(t)\|_h^2 \\
&\quad+(\epsilon_1^2+\epsilon_2^2)\|D_{-x}\omega_c(t)\|_+^2
\end{aligned}
\tag{59}
$$

and

$$
\begin{aligned}
&|((D_d(M_hT_h)-D_d(M_h\tilde{T}_h))D_{-x}c_h(t), D_{-x}\omega_c(t))_+| \\
&\quad\le |D_d'|_{max}\|\omega_T(t)\|_\infty\|D_{-x}c_h(t)\|_+\|D_{-x}\omega_c(t)\|_+ \\
&\quad\le \tfrac{1}{4\epsilon_3^2}(D_d')^2_{max}\|D_{-x}\omega_T(t)\|_+^2\|D_{-x}c_h(t)\|_+^2+\epsilon_3^2\|D_{-x}\omega_c(t)\|_+^2.
\end{aligned}
\tag{60}
$$

Then (58) is replaced by

$$
\begin{aligned}
&\|\omega_c(t)\|_h^2+\int_0^t e^{\int_s^t\left(\frac{\beta_2^2}{\epsilon_2^2}\|D_{-x}\tilde{T}_h(\mu)\|_+^2+2Q'_{max}\right)d\mu}\|D_{-x}\omega_c(s)\|_+^2ds \\
&\quad\le\frac{1}{\min\{1,2(\beta_3-\sum_{i=1}^3\epsilon_i^2)\}}\Big(\|\omega_c(0)\|_h^2e^{\int_0^t\left(\frac{\beta_2^2}{\epsilon_2^2}\|D_{-x}\tilde{T}_h(s)\|_+^2+2Q'_{max}\right)ds} \\
&\quad+\int_0^t e^{\int_s^t\left(\frac{\beta_2^2}{\epsilon_2^2}\|D_{-x}\tilde{T}_h(\mu)\|_+^2+2Q'_{max}\right)d\mu}\Big(\frac{1}{\epsilon_1^2}(v')^2_{max}\|c_h(s)\|_h^2 \\
&+\frac{1}{2\epsilon_3^2}(D_d')^2_{max}\|D_{-x}c_h(s)\|_+^2\Big)\|D_{-x}\omega_T(s)\|_+^2ds,\ t\in[0,T_f].
\end{aligned}
\tag{61}
$$

In this case, upper bounds for $\int_0^t\|D_{-x}\tilde{T}_h(s)\|_+^2ds$ can be easily obtained from (45). An estimate for $\int_0^t\|D_{-x}\omega_T(s)\|_+^2ds$ in established in (52) or (54). To conclude from (61) the stability of (35) and (36), we need to guarantee that $\|c_h(s)\|_h^2+\|D_{-x}c_h(s)\|_+^2$ is bounded a.e. in $(0,T_f)$, uniformly in $h\in\Lambda$. We observe that, from (48) or (50), $\|c_h(t)\|_h$, and $\int_0^t\|D_{-x}c_h(s)\|_+^2ds$ are bounded for all $t\in[0,T_f]$, uniformly in $h\in\Lambda$, and consequently $\|c_h(t)\|_h^2+\|D_{-x}c_h(t)\|_+^2$ is bounded a.e. in $(0,T_f)$, uniformly in $h\in\Lambda$. In fact, if $\int_0^t\|D_{-x}c_h(s)\|_+^2ds\le K,\forall t\in[0,T_f],\forall h\in\Lambda$, then $ess\sup_{(0,T_f)}\|D_{-x}c_h\|_+\le K,\forall h\in\Lambda$ (Theorem 2.14, [1]).

We remark that the assumption H_6 is verified if T_h and c_h are a second order approximations for T and c in $L^2(0,T_f,H^3(\Omega)\cap H^1_0(\Omega))$ in the following sense

$$\|E_T(t)\|_h^2 + \int_0^t \|D_{-x}E_T(s)\|_+^2 ds \le Ch^4_{max}, t\in[0,T_f], \tag{62}$$

and

$$\|E_c(t)\|_h^2 + \int_0^t \|D_{-x}E_c(s)\|_+^2 ds \le Ch^4_{max}, t\in[0,T_f], \tag{63}$$

where $E_T(t) = R_hT(t) - T_h(t)$, $E_c(t) = R_hc(t) - c_h(t)$, and under the assumption on the spatial grids of the sequence Λ

$$\frac{h^4_{max}}{h_{min}} \le Const, h\in\Lambda. \tag{64}$$

In fact,

$$\begin{aligned}\int_0^t \|D_{-x}T_h(s)\|_\infty^2 ds &\le 2\int_0^t \|D_{-x}E_h(s)\|_\infty^2 ds + 2\int_0^t \|\nabla T(s)\|_\infty^2 ds\\ &\le \frac{2}{h^2_{min}}\int_0^t \|D_{-x}E_h(s)\|_+^2 ds + 2\int_0^t \|\nabla T(s)\|_\infty^2 ds\\ &\le C\frac{h^4_{max}}{h^2_{min}} + 2\|T\|^2_{L^2(0,T_f,C^1(\Omega))}.\end{aligned}$$

In the following proposition we summarize our stability result for (35) and (36).

Proposition 2. *Under the assumptions* $H_1 - H_5$, H_2^*, H_3^* *and* H_5^*, *if* $\Omega_h, h\in\Lambda$, *satisfy (64),* $T_h, c_h \in C^1([0,T_f],W_{h,0}), h\in\Lambda$, *satisfy (62), (63), respectively, then there exists a set of positive constants* C_i, $i=1,\ldots,6$, *h-independent, such that, for* $\tilde{T}_h, \tilde{c}_h \in C^1([0,T_f],W_{h,0})$, *and* $\omega_T(t) = T_h(t) - \tilde{T}_h(t)$, $\omega_c(t) = c_h(t) - \tilde{c}_h(t)$, $h\in\Lambda$, *we have*

$$\|\omega_T(t)\|_h^2 + \int_0^t e^{2G'_{max}(t-s)}\|D_{-x}\omega_T(s)\|_+^2 ds \le C_1\|\omega_T(0)\|_h^2 \tag{65}$$

$$\begin{aligned}&\|\omega_c(t)\|_h^2 + \int_0^t e^{2Q'_{max}(t-s)}\|D_{-x}\omega_c(s)\|_+^2 ds\\ &\quad\le e^{C_2\|\tilde{T}_h(0)\|_h^2 + C_3}\Big(C_4\|\omega_c(0)\|_h^2 + \|\omega_T(0)\|_h^2\big(C_5 + C_6\|c_h(0)\|_h^2\big)\Big),\end{aligned} \tag{66}$$

for $t\in[0,T_f]$. ■

We establish in the next section the error estimates (62) and (63).

4. Convergence analysis

In this section our aim is to establish the upper bound (62) for the error $E_T(t) = R_hT(t) - T_h(t)$, and a similar upper bound for the error for the concentration $E_c(t) = R_hc(t) - c_h(t)$, where $T_h(t)$ and $c_h(t)$ are defined by (35) and (36), respectively. We remark that the results presented in [2] have an important role in what follows (see also [3],[7], [8]).

In what follows we use the following notation

$$(g)_h(x_i) = \frac{1}{|\Box_i|}\int_{\Box_i} g(x)dx, x_i \in \Omega_h,$$

with $\Box_i = [x_{i-1/2}, x_{i+1/2}]$.

4.1. Error estimate for the temperature $T_h(t)$ defined by (35). We have successively

$$\begin{aligned}(E_T'(t), E_T(t))_h &= ((T'(t))_h, E_T(t))_h - (T_h'(t), E_T(t))_h + \tau_d(t)\\ &= -(D_T(M_h(R_hT(t)))D_{-x}R_hT(t) - D_T(M_h(T_h(t)))D_{-x}T_h(t), D_{-x}E_T(t))_+\\ &+(R_hG(T(t)) - G(T_h(t)), E_T(t))_h\\ &+\tau_d(E_T(t)) + \tau_{D_T}(E_T(t)) + \tau_G(E_T(t)),\end{aligned} \tag{67}$$

where

$$\tau_d(t) = (R_hT'(t) - (T'(t))_h, E_h(t))_h, \tag{68}$$

$$\begin{aligned}\tau_{D_T}(E_T(t)) &= ((\nabla.(D_T(T(t))\nabla T(t)))_h, E_T(t))_h\\ &+(D_T(M_h(R_hT(t)))D_{-x}R_hT(t), D_{-x}E_T(t))_+\end{aligned}$$

and

$$\tau_G(E_T(t)) = ((G(T(t)))_h, E_T(t))_h - (R_hG(T(t)), E_T(t))_h.$$

In the next propositions we establish an estimate for the introduced error terms. By I_i we represent the interval (x_{i-1}, x_i).

Proposition 3. *If $T'(t) \in H^2(\Omega)$ then*

$$|\tau_d(t)| \le Const.\Big(\sum_{i=1}^N h_i^4\|T'(t)\|^2_{H^2(I_i)}\Big)^{1/2}\|D_{-x}E_T(t)\|_+. \tag{69}$$

Proof: See Theorem 3.1 of [2]. ∎

Proposition 4. *If $D_T \in W^{2,\infty}(\mathbb{R})$ and $T(t) \in H^3(\Omega) \cap H_0^1(\Omega)$, then*

$$|\tau_{D_T}(E_T(t))| \leq Const.\|D_T\|_{W^{2,\infty}(\mathbb{R})}\Big(\sum_{i=0}^{2}\|T(t)\|^i_{C^1(\overline{\Omega})}\Big)\Big(\sum_{i=1}^{N}h_i^4\|T(t)\|^2_{H^3(I_i)}\Big)^{1/2} \|D_{-x}E_T(t)\|_+. \tag{70}$$

Proof: For $\tau_{D_T}(t)$ we have

$$\begin{aligned}\tau_{D_T}(t) &= \Big(\big(\nabla.\big(D_T(T(t))\nabla T(t)\big)\big)_H, E_T(t)\Big)_h \\ &+(D_T(\hat{T}_h(t))D_{-x}R_hT(t), D_{-x}E_T(t))_+ \\ &-(D_T(\hat{T}_h(t))D_{-x}R_hT(t), D_{-x}E_T(t))_+ \\ &+(D_T(M_h(R_hT(t)))D_{-x}R_hT(t), D_{-x}E_T(t))_+ \\ &:= \tau_1(t) + \tau_2(t),\end{aligned}$$

where $\hat{T}_h(t)(x_i) = T(x_{i-1/2}, t)$.

(1) An estimate for $\tau_1(t)$ is obtained using Theorem 3.1 of [2]

$$|\tau_1(t)| \leq Const.\Big(\sum_{i=1}^{N}h_i^4\|D_T((T(t))\nabla T(t)\|^2_{H^2(I_i)}\Big)^{1/2}\|D_{-x}E_T(t)\|_+.$$

(2) To get an estimate for $\tau_2(t)$ we start by remarking that the Bramble-Hilbert lemma allows us to obtain for

$$\sigma(x_i, t) = T(x_{i-1/2}, t) - \frac{1}{2}\Big(T(x_{i-1}, t) + T(x_i, t)\Big)$$

the following estimate

$$|\sigma(x_i, t)| \leq Const.h_i\int_{x_{i-1}}^{x_i}|\Delta T(x, t)|dx,$$

and then we get

$$|\tau_2(t)| \leq Const.\|D'_T\|_\infty\Big(\sum_{i=1}^{N}h_i^4\|T(t)\|_{C^1(\overline{I}_i)}\|T(t)\|^2_{H^2(I_i)}\Big)^{1/2} \|D_{-x}E_T(t)\|_+.$$

We conclude for $|\tau_{D_T}(E_T(t))|$ the next estimate

$$\begin{aligned}|\tau_{D_T}(E_T(t))| \ &\leq Const.\Big(\sum_{i=1}^{N} h_i^4 \|D_T(T(t))\nabla T(t)\|^2_{H^2(I_i)} \\ &\quad + \|D'_T(t)\|_\infty \sum_{i=1}^{N} h_i^4 \|T(t)\|_{C^1(\overline{I_i})} \|T(t)\|^2_{H^2(I_i)}\Big)^{1/2} \|D_{-x}E_T(t)\|_+,\end{aligned}$$

that lead to (70).

■

Proposition 5. *If $G \in W^{2,\infty}(\mathbb{R})$ and $T(t) \in H^2(\Omega) \cap H^1_0(\Omega)$, then*

$$\begin{aligned}|\tau_G(E_T(t))| \ &\leq Const. \max\{\beta_1, \|G\|_{W^{2,\infty}(\mathbb{R})}\}\Big(\sum_{i=0}^{1} \|T(t)\|^i_{C^1(\overline{\Omega})}\Big) \\ &\quad \Big(\sum_{i=1}^{N} h_i^4 \|T(t)\|^2_{H^2(I_i)}\Big)^{1/2} \|D_{-x}E_T(t)\|_+.\end{aligned} \tag{71}$$

Proof: See Theorem 3.1 of [2]. ■

In the next result we establish the upper bound for $E_T(t)$:

Theorem 1. *If*

$$T \in L^2(0, T_f, H^3(\Omega) \cap H^1_0(\Omega)) \cap H^1(0, T_f, H^2(\Omega)),$$
$$R_h T, T_h \in C^1([0, T_f], W_{h,0}),$$

the coefficient functions D_T and G satisfy the assumptions H_1, H_2, respectively, as well as the assumption of Propositions 4 and 5. Then for ϵ such that $\beta_0 - 4\epsilon^2 > 0$ the error $E_T(t) = R_h T(t) - T_h(t)$ satisfies the following

$$\begin{aligned}&\|E_T(t)\|^2_h + \int_0^t e^{\int_s^t \left(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(\mu)\|^2_\infty + 2G'_{max}\right)d\mu} \|D_{-x}E_T(s)\|^2_+ ds \\ &\quad \leq \frac{1}{\min\{1, 2(\beta_0 - 4\epsilon^2)\}} e^{\int_0^t \left(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(\mu)\|^2_\infty + 2G'_{max}\right)ds} \Big(\|E_T(0)\|^2_h \\ &+ \frac{1}{2\epsilon^2}\int_0^t e^{-\int_0^s \left(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(\mu)\|^2_\infty + 2G'_{max}\right)d\mu} \tau_T(s) ds\Big), t \in [0, T_f],\end{aligned} \tag{72}$$

where

$$\tau_T(t) = Const.\Big(\sum_{i=0}^{2} \|T(t)\|^i_{C^1(\overline{\Omega})}\Big)^2 \sum_{i=1}^{N} h_i^4 \Big(\|T(t)\|^2_{H^3(I_i)} + \|T'(t)\|^2_{H^2(I_i)}\Big).$$

Proof: From (67) and Propositions 3, 4 and 5, we easily get

$$\begin{aligned}&\frac{1}{2}\frac{d}{dt}\|E_T(t)\|_h^2+\beta_0\|D_{-x}E_T(t)\|_+^2\\&\quad\le\sqrt{2}|D'_T|_{max}\|E_T(t)\|_h\|D_{-x}R_hT(t)\|_\infty\|D_{-x}E_T(t)\|_+\\&\quad+G'_{max}\|E_T(t)\|_h^2+\frac{1}{4\epsilon^2}\tau_T(t)+3\epsilon^2\|D_{-x}E_T(t)\|_+^2,\end{aligned}\tag{73}$$

where $\epsilon\neq 0$ is an arbitrary constant.
The inequality (73) leads to

$$\begin{aligned}&e^{-\int_0^t\left(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(\mu)\|^2_\infty+2G'_{max}\right)d\mu}\frac{d}{dt}\|E_T(t)\|_h^2\\&+2(\beta_0-4\epsilon^2)e^{-\int_0^t\left(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(s)\|^2_\infty+2G'_{max}\right)ds}\|D_{-x}E_T(t)\|_+^2\\&\quad\le e^{-\int_0^t\left(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(s)\|^2_\infty+2G'_{max}\right)ds}\Big(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(t)\|^2_\infty\\&+2G'_{max}\Big)\|E_T(t)\|_h^2+\frac{1}{2\epsilon^2}e^{-\int_0^t\left(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}R_hT(s)\|^2_\infty+2G'_{max}\right)ds}\tau_T(t),\end{aligned}\tag{74}$$

for $t\in[0,T_f]$. Finally, choosing ϵ such that $\beta_0-4\epsilon^2>0$ and considering the continuous imbedding of $H^3(\Omega)$ in $C^1(\overline{\Omega})$, we conclude (72).

■

Corollary 1. *Under the assumptions of Theorem 1, if $T_h(0)=R_hT(0)$ then there exists a positive constant C such that the error $E_T(t)$ satisfies*

$$\|E_T(t)\|_h^2+\int_0^t e^{2G'_{max}(t-s)}\|D_{-x}E_T(s)\|_{h,+}^2ds\le Ch^4_{max},t\in[0,T_f].$$

If the sequence Λ of the spatial vectors h satisfies the assumption (64), then the sequence of approximations for the temperature $T_h, h\in\Lambda$, is uniformly bounded in the sense

$$\|T_h(t)\|_\infty\le C,\int_0^t e^{2G'_{max}(t-s)}\|D_{-x}T_h(s)\|_+^2ds\le C,\ t\in[0,T_f],h\in\Lambda.$$

4.2. Error estimate for the concentration $c_h(t)$ defined by (36). For the error $E_c(t) = R_hc(t) - c_h(t)$ holds the following

$$
\begin{array}{l}
(E_c'(t), E_c(t))_H = ((c'(t))_h, E_c(t))_h - (c_h'(t), E_c(t))_h + \tau_d(E_c(t)) \\
= -(D_d(M_h(R_hT(t)))D_{-x}R_hc(t) - D_d(M_h(T_h(t)))D_{-x}c_h(t), D_{-x}E_c(t))_+ \\
+(M_h(R_h(v(T(t))c(t))), D_{-x}E_c(t))_+ - (M_h(v(T_h(t))c_h(t)), D_{-x}E_c(t))_+ \\
\quad +(R_hQ(c(t)) - Q(c_h(t)), E_c(t))_h \\
\quad +\tau_d(E_c(t)) + \tau_{D_d}(E_c(t)) + \tau_v(E_c(t)) + \tau_Q(E_c(t)),
\end{array} \tag{75}
$$

where $\tau_d(E_c(t))$ is defined by(68) with $T(t)$ and $E_T(t)$ replaced by $c(t)$ and $E_c(t)$, respectively,

$$
\begin{array}{ll}
\tau_{D_d}(E_c(t)) & = ((\nabla.(D_d(T(t))\nabla c(t)))_h, E_c(t))_h \\
& +(D_d(M_h(R_hT(t)))D_{-x}R_hc(t), D_{-x}E_c(t))_+,
\end{array}
$$

$$
\begin{array}{ll}
\tau_v(E_c(t)) & = -(\big(\nabla.(v(T(t))c(t))\big)_h, E_c(t))_h \\
& -(M_h(R_h(v(T(t))c(t))), D_{-x}E_c(t))_+,
\end{array}
$$

and

$$
\tau_Q(E_c(t)) = ((Q(c(t)))_h, E_c(t))_h - (R_hQ(c(t)), E_c(t))_h.
$$

As in Proposition 3, for $\tau_d(E_c(t))$ we have

$$
|\tau_d(E_c(t))| \leq \Big(\sum_{i=1}^{N} h_i^4 \|c'(t)\|^2_{H^2(I_i)}\Big)^{1/2} \|D_{-x}E_c(t)\|_+. \tag{76}
$$

For $\tau_Q(E_c(t))$ we easily get

$$
\begin{array}{ll}
|\tau_Q(E_c(t))| & \leq Const.\|R\|_{W^{2,\infty}(\mathbb{R})}\Big(\sum_{i=0}^{1} \|c(t)\|^i_{C^1(\overline{\Omega})}\Big)\Big(\sum_{i=1}^{N} h_i^4 \|c(t)\|^2_{H^2(I_i)}\Big)^{1/2} \\
& \qquad \|D_{-x}E_c(t)\|_+.
\end{array} \tag{77}
$$

We study now $\tau_{D_d}(E_c(t))$ and $\tau_v(E_c(t))$.

Proposition 6. *If* $D_d \in W^{2,\infty}(\mathbb{R})$, $T(t) \in H^2(\Omega) \cap H_0^1(\Omega)$ *and* $c(t) \in H^3(\Omega) \cap H_0^1(\Omega)$, *then*

$$\begin{aligned} |\tau_{D_d}(E_T(t))| \; & \leq Const.\|D_d\|_{W^{2,\infty}(\mathbb{R})}\Big(\Big(\sum_{i=0}^{2}\|T(t)\|^i_{C^1(\overline{\Omega})}\Big)^2\sum_{i=1}^{N}h_i^4\|c(t)\|^2_{H^3(I_i)} \\ & + \|c(t)\|^2_{C^1(\overline{\Omega})}\sum_{i=1}^{N}h_i^4\|T(t)\|^2_{H^2(I_i)}\Big)^{1/2}\|D_{-x}E_c(t)\|_{+}. \end{aligned} \tag{78}$$

Proof: The proof follows the proof of Proposition 4. ■

Proposition 7. *If* $T(t), c(t) \in H^2(\Omega) \cap H_0^1(\Omega)$ *then*

$$\begin{aligned} |\tau_{v}(E_T(t))| \; & \leq Const.\|v\|_{W^{2,\infty}(\mathbb{R})}\Big(\Big(\sum_{i=0}^{2}\|T(t)\|^i_{C^1(\overline{\Omega})}\Big)^2\sum_{i=1}^{N}h_i^4\|c(t)\|^2_{H^2(I_i)} \\ & + \|c(t)\|^2_{C^0(\overline{\Omega})}\sum_{i=1}^{N}h_i^4\|T(t)\|^2_{H^2(I_i)}\Big)^{1/2}\|D_{-x}E_c(t)\|_{+}. \end{aligned} \tag{79}$$

Proof: See Theorem 3.1 of [2]. ■

Theorem 2. *Let us suppose that*

$$T, c \in L^2(0, T_f, H^3(\Omega) \cap H_0^1(\Omega)) \cap H^1(0, T_f, H^2(\Omega)),$$

$$R_hT, R_hc, T_h, c_h \in C^1([0, T_f], W_{h,0}),$$

the coefficient function D_T *and* G *satisfy the assumptions* H_1, H_2, *respectively, and* v *and* D_d *satisfy the assumption* H_3, H_4, *respectively. If the sequence* Λ *of the spatial vectors* h *satisfies the assumption (64), then for the error* $E_c(t) = R_hc(t) - c_h(t)$ *we have*

$$\begin{aligned} &\|E_c(t)\|_h^2 + \int_0^t e^{\int_s^t \left(\frac{1}{\epsilon^2}\beta_2^2\|T_h(\mu)\|_\infty^2 + 2Q'_{max}\right)d\mu}\|D_{-x}E_c(s)\|_+^2 ds \\ &\quad \leq \frac{1}{\min\{1, 2(\beta_3 - 7\epsilon^2)\}} e^{\int_0^t \left(\frac{1}{\epsilon^2}\beta_2^2\|T_h(s)\|_\infty^2 + 2Q'_{max}\right)ds}\Big(\|E_c(0)\|_h^2 \\ &+ \int_0^t e^{-\int_0^s \left(\frac{1}{\epsilon^2}\beta_2^2\|T_h(\mu)\|_\infty^2 + 2Q'_{max}\right)d\mu}\Big(\frac{1}{\epsilon^2}(D'_T)^2_{max}\|D_{-x}c(s)\|_\infty^2 \\ &+ \frac{1}{\epsilon^2}(v')^2_{max}\|c(s)\|_\infty^2\Big)\|E_T(s)\|_h^2 ds + \frac{1}{\epsilon^2}\int_0^t e^{\int_0^s \left(\frac{1}{\epsilon^2}\beta_2^2\|T_h(\mu)\|_\infty^2 + 2Q'_{max}\right)d\mu}\tau_c(s)ds, t \in [0, T_f], \end{aligned} \tag{80}$$

where $\epsilon \neq 0$ is such that $\beta_3 - 7\epsilon^2 > 0$, $\|E_T(t)\|_h^2$ is bounded in (72) and

$$\begin{aligned}
\tau_c(t) &= C\Big(\sum_{i=1}^{N} h_i^4 \|c'(t)\|^2_{H^2(I_i)} \\
&\quad + \big(\sum_{i=0}^{1} \|c(t)\|^i_{C^1(\overline{\Omega})}\big)^2 \sum_{i=1}^{N} h_i^4 \big(\|c(t)\|^2_{H^2(I_i)} + \|T(t)\|^2_{H^2(I_i)}\big) \\
&\quad + \big(\sum_{i=0}^{2} \|T(t)\|^i_{C^1(\overline{\Omega})}\big)^2 \sum_{i=1}^{N} h_i^4 \|c(t)\|^2_{H^3(I_i)} \Big).
\end{aligned}$$

Proof: From Theorem 1, $\|T_h(t)\|_\infty, h \in \Lambda$, is uniformly bounded in $[0, T_f]$. From (75), we easily get

$$\begin{aligned}
&\tfrac{1}{2}\|E_c(t)\|_h^2 + \beta_3 \|D_{-x}E_c(t)\|_+^2 \\
&\quad \leq \sqrt{2}|D_d'|_{max}\|D_{-x}c(t)\|_\infty \|E_T(t)\|_h \|D_{-x}E_c(t)\|_+^2 \\
&\quad + |v'|_{max}\sqrt{2}\|E_T(t)\|_h \|c(t)\|_\infty \|D_{-x}E_c(t)\|_+ \\
&\quad + \sqrt{2}\beta_2 \|T_h(t)\|_\infty \|E_c(t)\|_h \|D_{-x}E_c(t)\|_+ \\
&\quad + Q'_{max}\|E_c(t)\|_h^2 + \tau_d(E_c(t)) + \tau_{D_d}(E_c(t)) + \tau_v(E_c(t)) + \tau_Q(E_c(t)).
\end{aligned}$$

Consequently, $E_c(t)$ satisfies

$$\begin{aligned}
&\frac{d}{dt}\|E_c(t)\|_h^2 + 2(\beta_3 - 7\epsilon^2)\|D_{-x}E_c(t)\|_+^2 \\
&\quad \leq \big(\frac{1}{\epsilon^2}(D_d')^2_{max}\|D_{-x}c(t)\|^2_\infty + \frac{1}{\epsilon^2}(v')^2_{max}\|c(t)\|^2_\infty\big)\|E_T(t)\|_h^2 \\
&\quad + \big(\frac{1}{\epsilon^2}\beta_2^2\|T_h(t)\|^2_\infty + 2Q'_{max}\big)\|E_c(t)\|_h^2 + \frac{1}{\epsilon^2}\tau_c(t),
\end{aligned} \tag{81}$$

where $\epsilon \neq 0$ is an arbitrary constant, and

$$\begin{aligned}
\tau_c(t) &= Const.\Big(\sum_{i=1}^{N} h_i^4 \|c'(t)\|^2_{H^2(I_i)} \\
&\quad + \big(\sum_{i=0}^{1} \|c(t)\|^i_{C^1(\overline{\Omega})}\big)^2 \sum_{i=1}^{N} h_i^4 \big(\|c(t)\|^2_{H^2(I_i)} + \|T(t)\|^2_{H^2(I_i)}\big) \\
&\quad + \big(\sum_{i=0}^{2} \|T(t)\|^i_{C^1(\overline{\Omega})}\big)^2 \sum_{i=1}^{N} h_i^4 \|c(t)\|^2_{H^3(I_i)} \Big).
\end{aligned}$$

The inequality (81) is equivalent to the following one

$$\begin{aligned}&\|E_c(t)\|_h^2 + 2(\beta_3 - 7\epsilon^2)\int_0^t \|D_{-x}E_c(s)\|_+^2 ds\\ &\quad \leq \|E_c(0)\|_h^2 + \int_0^t \big(\frac{1}{\epsilon^2}(D_d')^2_{max}\|D_{-x}c(s)\|_\infty^2 + \frac{1}{\epsilon^2}(v')^2_{max}\|c(s)\|_\infty^2\big)\|E_T(s)\|_h^2 ds\\ &\quad + \int_0^t \big(\frac{1}{\epsilon^2}\beta_2^2\|T_h(s)\|_\infty^2 + 2Q'_{max}\big)\|E_c(s)\|_h^2 ds + \frac{1}{\epsilon^2}\int_0^t \tau_c(s)ds,\end{aligned}$$

that leads to (80).

■

By Corollary 1, for the error $E_T(t)$ we have the following

$$\|E_T(t)\|_h^2 \leq Ch_{max}^4, t \in [0, T_f].$$

Then, from Theorem 2, we finally conclude the next estimate.

Corollary 2. *Under the assumptions of Theorems 1 and 2, if* $T_h(0) = R_hT(0)$, $c_h(0) = R_hc(0)$, *then there exists a positive constant* C *such that the error* $E_c(t)$ *satisfies*

$$\|E_c(t)\|_h^2 + \int_0^t e^{2Q'_{max}(t-s)}\|D_{-x}E_c(s)\|_+^2 ds \leq Ch_{max}^4, t \in [0, T_f].$$

5. Numerical simulation

5.1. Convergence rates. In this section our goal is to illustrate the main results of this work: Theorems 1 and 2. We consider $T_f = 0.1$, and we introduce in $[0, T_f]$ the uniform grid $\{t_m, m = 0, \ldots, M\}$ with stepsize Δt such that $\Delta t \leq Const.h_{max}^2$.
As we intent to illustrate the convergence rates established in Theorems 1 and 2, we consider the the differential equations (4) and (5) with reaction terms $f_2(t)$ and $f_1(t)$, respectively. These new reactive terms induce in (35), (36), the new terms $((f_1(t))_h, u_h)_h$ and $((f_2(t))_h, w_h)_h$, respectively, or equivalently in the semi-discrete FD problems (37) and (38) the new reactive terms $(f_1(t))_h$ and $(f_2(t))_h$, respectively.
To avoid the computation of the solution of non-linear systems, the new version of the semi-discrete FE problem (35), (36), or equivalently the new version of the semi-discrete FD problem (37) and (38), are integrated in time using Euler's method following an implicit-explicit approach (IMEX

approach)

$$\begin{cases} (T_h^{m+1}, \phi_h)_h & +\Delta t(D_T(M_hT_h^m)D_{-x}T_h^{m+1}, D_{-x}\phi_h)_+ = (T_h^m, \phi_h)_h \\ & +\Delta t(G(T_h^m), \phi_h)_h + \Delta t((f_1(t_m))_h, \phi_h)_h, \\ & m = 0, \dots, M-1, \forall \phi_h \in W_{h,0}, \\ T_h^0 = R_hT_0, & \end{cases} \tag{82}$$

and

$$\begin{cases} (c_h^{m+1}, \psi_h)_h - \Delta t(M_h(v(T_h^m)c_h^{m+1}), D_{-x}\psi_h)_+ + \Delta t(D_d(M_hT_h^m)D_{-x}c_h^{m+1}, D_{-x}\psi_h)_+ \\ \quad = (c_h^m, \psi_h) + \Delta t(Q(c_h^m), \psi_h)_h + \Delta t((f_2(t_m))_h, \psi_h)_h, \\ \qquad m = 0, \dots, M-1, \forall \psi_h \in W_{h,0}, \\ c_h^0 = R_hc_0. \end{cases} \tag{83}$$

The fully discrete FE discretizations (82), (83) are equivalent to the following FD discretizations

$$\begin{cases} T_h^{m+1} - \Delta t(D_x^*\Big(D_T(M_hT_h^m)D_{-x}T_h^{m+1}\Big) = T_h^m + \Delta tG(T_h^m) + \Delta t(f_1)_h, \\ \qquad\qquad\qquad\qquad\qquad\qquad \text{in } \Omega_h,\ m = 0, \dots, M-1, \\ T_h^0 = R_hT_0 \,\text{in}\, \Omega_h, \\ T_h^m = 0 \,\text{on}\, \partial\Omega_h, m = 1, \dots, M, \end{cases} \tag{84}$$

$$\begin{cases} c_h^{m+1} + \Delta tD_c\big((v(T_h^m)c_h^{m+1}) - \Delta tD_x^*(D_d(M_hT_h^m)D_{-x}c_h^{m+1}) = c_h^m \\ \qquad\qquad +\Delta tQ(c_h^m) + \Delta t(f_2)_h \text{ in } \Omega_h,\ m = 0, \dots, M-1, \\ c_h^0 = R_hc_0 \,\text{in}\, \Omega_h, \\ c_h^m = 0 \,\text{on}\, \partial\Omega_h, m = 1, \dots, M. \end{cases} \tag{85}$$

In the error tables that we present in what follows, we illustrate the behaviour of the errors

$$Error_{\ell,h} = \max_{j=1,\cdots,M}\Big(\|E_\ell^j\|_h^2 + \Delta t\sum_{j=1}^{M}\|D_{-x}E_\ell^j\|_+^2\Big), \ell = T, c,$$

where

$$E_\ell^j = R_h\ell(t_j) - \ell_h^j, j = 1, \dots, M,$$

and ℓ_h^j is the approximation for $\ell_h(t_j)$ defined by the IMEX method (82), (83) (or (84), (85)). We also include the convergence rates $Rate_\ell$ defined considering the following formula

$$Rate_\ell = \frac{\log\left(\frac{Error_{\ell,h_{max,i}}}{Error_{\ell,h_{max,i+1}}}\right)}{\log\left(\frac{h_{max,i}}{h_{max,i+1}}\right)}, \ \ell = T, c,$$

where $h_{max,i}$ and $h_{max,i+1}$ are defined by two consecutive grids $\Omega_{h,i}$ and $\Omega_{h,i+1}$.

We consider $D_T(T) = D_T$, with $D_T = 10^{-3}(cm^2/s)$, and the diffusion coefficient for the concentration given by the Arrhenius equation (1), with $R = 8.3144621$, $E_a = 1.60217662 \times 10^{-19}$, $D_0 = 10^{-1}(cm^2/s)$. Moreover, to simplify, we assume that the convective velocity is defined by $v(T) = bT(cm/s)$, where $b = 10^{-1}(cm/s^oK)$. We also take $G = Q = 0$ and $\Delta t = 1^{-6}(s)$.

In the first example we consider f_1 and f_2 such that the differential system (4), (5) has the following solution

$$\begin{aligned} &T(x,t) = e^{-D_T t} sin(\pi x), \\ &c(x,t) = e^{-t} sin(2\pi x), \ \text{for } x \in [0,1], t \in [0, T_f]. \end{aligned} \tag{86}$$

In Table 1 we include the errors for the numerical approximations for T and c obtained with (82), (83) (or (84), (85)), and the correspondent convergence rates $Rate_\ell, \ell = T, c$. The results included in this table illustrate Theorems 1 and 2 when T and c are smooth functions.

N_{points}	h_{max}	E_T	R_T	E_c	R_c
40	3.75×10^{-2}	2.66001×10^{-5}	——	4.33994×10^{-3}	——
80	1.875×10^{-2}	1.16484×10^{-5}	1.19130	1.12487×10^{-3}	1.94791
160	9.375×10^{-3}	3.75280×10^{-6}	1.63409	2.82498×10^{-4}	1.99345
320	4.6875×10^{-3}	1.0090×10^{-6}	1.89504	7.09491×10^{-5}	1.99338
640	2.34375×10^{-3}	2.56835×10^{-7}	1.97401	1.77873×10^{-5}	1.99594
1280	1.171875×10^{-3}	6.44969×10^{-8}	1.99354	4.48864×10^{-6}	1.98649

Table 1. Convergence rates for the numerical approximations for the smooth solutions (86).

To see the sharpness of our convergence results in what concerns the smoothness assumptions for the solutions, we consider now the differential system (4), (5) with solution

$$\begin{aligned} &T(x,t) = e^{-D_T t} sin(\pi x)|2x-1|^\alpha, \\ &c(x,t) = e^{-t} x(1-x)|2x-1|^\alpha, \ \text{for } x \in [0,1], t \in [0, T_f]. \end{aligned} \tag{87}$$

We observe that $T(t), c(t) \in H^3(\Omega)$ for $\alpha > 3$, and $T(t), c(t) \in H^2(\Omega)$ for $3 \leq \alpha > 2$. In Tables 2 and 3 we include the errors and the correspondent convergence rates obtained for $\alpha = 3.1$ and $\alpha = 2.1$, respectively. The results show that when the solutions T and c do not satisfy the smoothness assumption $T(t), c(t) \in H^3(\Omega)$, then we lose the second order convergence rates.

N_{points}	h_{max}	E_T	R_T	E_c	R_c
40	3.75×10^{-2}	8.02419×10^{-5}	——	5.20569×10^{-4}	——
80	1.875×10^{-2}	3.37646×10^{-5}	1.24885	1.33263×10^{-4}	1.96581
160	9.375×10^{-3}	1.06791×10^{-5}	1.66072	3.37786×10^{-5}	1.98009
320	4.6875×10^{-3}	2.88317×10^{-6}	1.88907	8.49696×10^{-6}	1.99109
640	2.34375×10^{-3}	7.39408×10^{-7}	1.96321	2.13042×10^{-6}	1.99581
1280	1.171875×10^{-3}	1.86910×10^{-7}	1.98403	5.32633×10^{-7}	1.99992

TABLE 2. Convergence rates for the α-solution numerical approximation with $\alpha = 3.1$

N_{points}	h_{max}	E_T	R_T	E_c	R_c
40	3.75×10^{-2}	1.11053×10^{-4}	——	4.07632×10^{-4}	——
80	1.875×10^{-2}	5.09896×10^{-5}	1.12297	1.46949×10^{-4}	1.47195
160	9.375×10^{-3}	2.06318×10^{-5}	1.30533	6.00531×10^{-5}	1.29101
320	4.6875×10^{-3}	9.77867×10^{-6}	1.07715	2.65040×10^{-5}	1.18003
640	2.34375×10^{-3}	5.36280×10^{-6}	0.86665	1.21129×10^{-5}	1.12967
1280	1.171875×10^{-3}	2.90522×10^{-6}	0.88434	5.61021×10^{-6}	1.11041

TABLE 3. Convergence rates for the α-solution numerical approximation with $\alpha = 2.1$

5.2. Qualitative behaviour. In this section we illustrate the effectiveness of the temperature as a drug release enhancer. We consider an isotropic and homogeneous tissue where a drug is initially dispersed. The assumptions on the properties of the tissue allow us to replace the 3D drug release problem by a 1D problem. To enhance the drug transport through the tissue, a localized heat source term is assumed in contact with the tissue at the boundaries.

It is reported in the literature that the increase of the temperature increases the tissue permeability, body fluid circulation, blood vessel wall permeability, rate-limiting membrane permeability and drug solubility. All these individual contributions are macroscopically taken into account in the convective velocity $v(T)$ and in the drug diffusion coefficient $D_d(T)$ that we assume to be given by given by the Arrhenius equation (1).

We consider that the heat sources are applied at the boundaries of the domain $\Omega = (0, 1)$. Initially, the drug concentration is defined by $T(x, 0) = x(1-x)$ (g/cm^3) , $x \in (0, 1)$. We consider $G = 0$ and $T_f = 10^4$ (s), $D_T = 10^{-7}$ (cm^2/s), $D_0 = 10^{-4}$ (cm^2/s). We take $\Delta t = 10^{-1}$ (s) and $h = 1.25 \times 10^{-2}$ (cm).

- In what follows we consider that the heat is generated by $T(0, t) = T(1, t) = 310+0.1t$ (^oK) for an activation energy E_a such that $E_a/R = 4.43 \times 10^2$ (s), and $v(t) = 0$.

  In Figure 1 we plot the temperature curves for different times. As the heat sources are localized at the boundaries, we observe an increasing of the temperature from the boundaries to the interior. The evolution of the concentration when the diffusion coefficient depends on the temperature is illustrated in Figure 2. In this case we consider the temperature given in Figure 1. As the time increases, an increasing on the transport near the left and right boundaries is observed. This fact is consequence of the increasing on the temperature observed in these zones. The correspondent released mass $M_r(t)$ is plotted in Figure 3. The released mass increases when the drug transport is enhanced by the temperature.

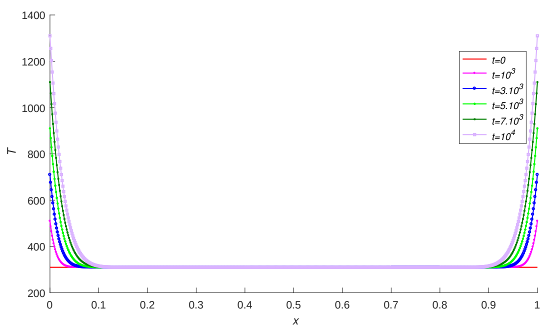

FIGURE 1. Evolution of the temperature for $T(0, t) = T(1, t) = 310 + 0.1t$.

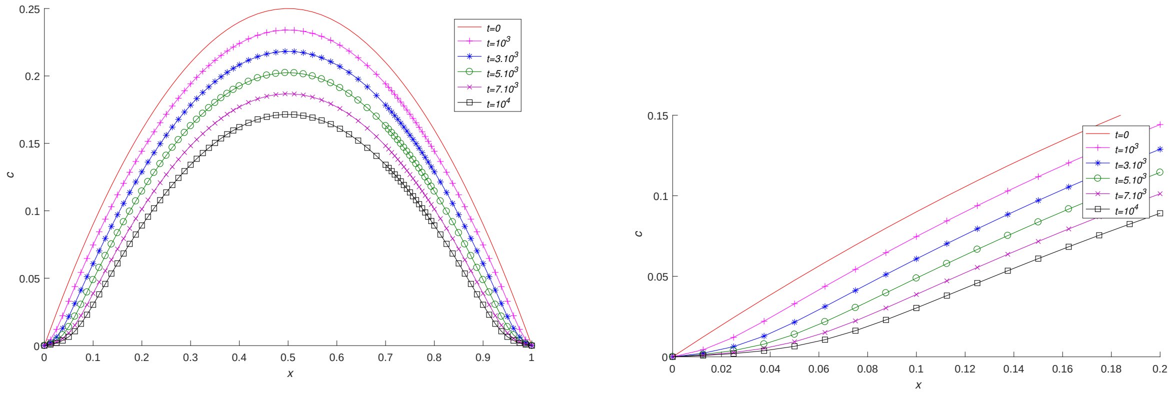

FIGURE 2. Evolution of the temperature when the heat sources are defined by $T(0,t) = T(1,t) = 310 + 0.1t$. The right figure is a zoom of the left figure.

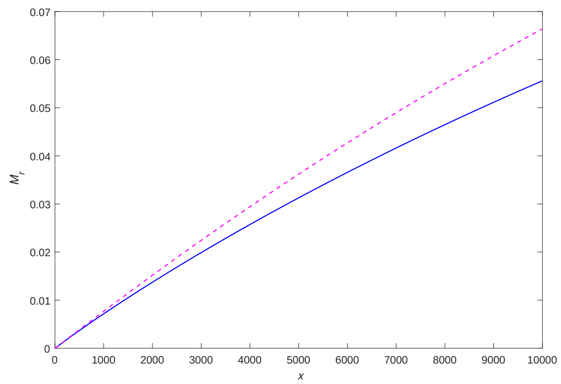

FIGURE 3. Evolution of the released drug masses: under the effect of the temperature (dashed line); without the temperature effect (continuous line) for the diffusion coefficient $D = 10^{-4}$ and $v = 0$.

- We assume now that the heat is generated by $T(0,t) = T(1,t) = 310 + 5 \times 10^{-4}t$ (^oK), for $t > 0$, and the heat induces a convective transport given by $v(T) = bT$, with $b = 5 \times 10^{-4}$, (cm/s^oK). We assume that the activation energy E_a is such that $E_a/R = 10^3$ (s). Figure 4 illustrates the behaviour of the temperature. A we can see, it increases when t increases from the boundaries, where we have the heat source, to the interior. In Figure 5 we plot the evolution of the corresponding drug concentration. As the heat generates a convective term, we observe a displacement of the highest concentration values from the left to the right and such displacement increases with time. The behaviour of the released drug mass $M_r(t)$ is illustrated in Figure 6. The heat, generated by the sources applied at the boundaries of the domain, increases the transport from the left to the right and, consequently, it increases the released drug.

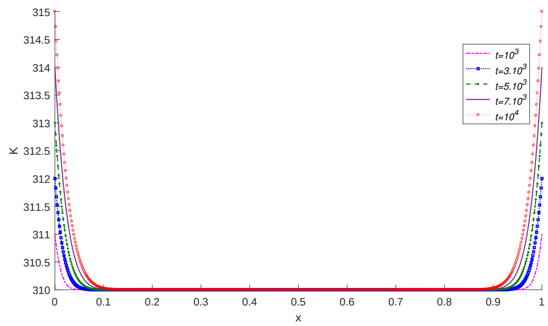

FIGURE 4. Evolution of the temperature for $T(0,t) = T(1,t) = 310 + 5 \times 10^{-4}t$.

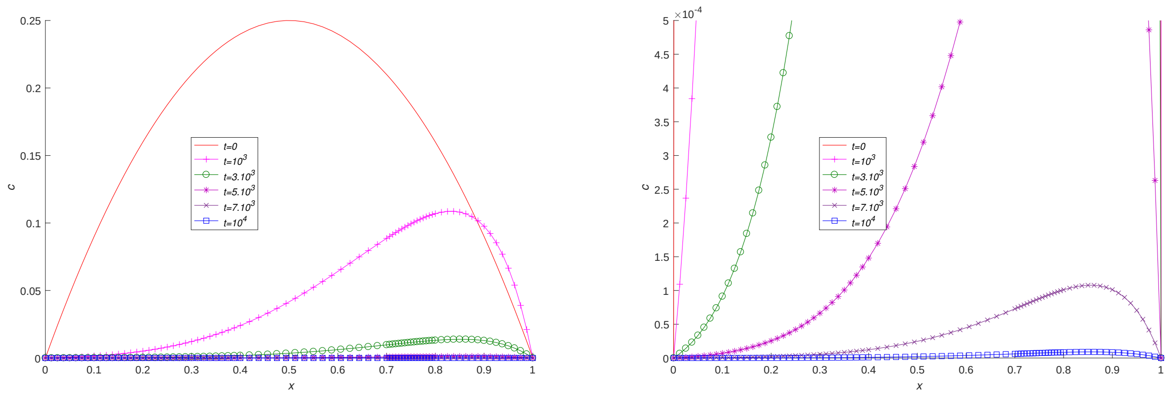

FIGURE 5. Evolution of the concentration when the heat source is given by $T(0,t) = T(1,t) = 310 + 5 \times 10^{-4}t$. The right figure is a zoom of the left figure.

6. Conclusions

The use of the heat as a stimulus to enhance drug release is nowadays a common approach in several medical applications (see [5], [6], [12], [18] and

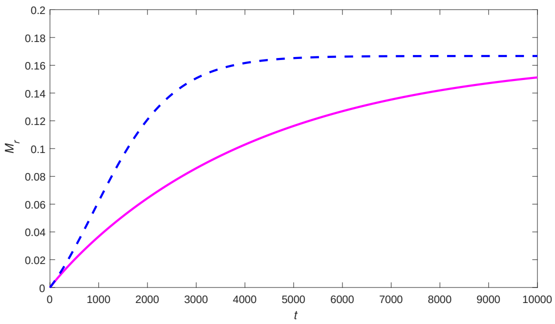

FIGURE 6. Evolution of the released drug masses: under the effect of the temperature (dashed line); without the temperature effect (continuous line) for the diffusion coefficient $D = 10^{-4}$ and $v = 0$.

[21]). Mathematically, the drug release enhanced by the temperature is described by a diffusion-reaction equation for the temperature and a convection-diffusion-reaction equation for the drug, where the convective and the drug diffusion coefficients depend on the temperature.

In this work we propose a numerical method to compute the temperature and the drug concentration. The method is based on the piecewise linear finite element method, combined with special quadrature rules. It leads to second order numerical approximations for the temperature and for the concentration provided that both solutions are in $H^3(\Omega) \cap H^1_0(\Omega)$ (Theorems 1 and 2). The proposed method mimics the continuous coupling in what concerns the stability behaviour as it was shown, in Section 2, for the continuous coupling, and, in Section 3.2, for the numerical coupling problem. The main stability result - Proposition 2- establishes that the fully discrete finite element method (35), (36) or, equivalently, the finite difference method (37), (38) is stable. This result was proved under assumption H_6 that is consequence of the second convergence order established in Theorems 1 and 2.

We reinforce the fact that our convergence analysis in not based on the classical approach: consistency and stability imply convergence. The error analysis in based on the analysis of the error equation and on the use of the approach introduced by one of the authors in [2], and used later for the coupling between an elliptic equation and an integro-differential equation in

[3], and for the coupling between an hyperbolic equation and a convection-diffusion equation that arises in models for drug delivery enhanced by ultrasons in [8].

Numerical results were included to illustrate the main convergence results. The results presented in Tables 1, 2 and Table 3 illustrate the sharpness of our results in what concerns the smoothness assumptions for the temperature and concentration.

The numerical results presented in Figures 3, 6 shows that the use of heat to enhance drug release is in fact an effective procedure.

7. Acknowledgements

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References

[1] R. Adams, Sobolev Spaces, 2^{nd} edition, Elsevier, 2003.

[2] S. Barbeiro, J.A: Ferreira, R. Grigorieff, Supraconvergence of a finite difference scheme for solutions in $H^s(0, L)$, IMA Journal of Numerical Analysis, 25 (2005), 797–811.

[3] S. Barbeiro,S. Bardeji, J.A: Ferreira, L. Pinto, Non-Fickian convection-diffusion models in porous media, Numerische Mathematik, 138 (2018), 869–904.

[4] S. Becker, Skin electroporation with passive transdermal transport theory: a review and a suggestion for future numerical model development, Journal of Heat Transfer, 133 (2011), 011011.

[5] S. Chowdhury, T. Lee, J. Willmann, Ultrasound-guided drug delivery in cancer, Ultrasonography, 36 (2017), 171–184.

[6] O. Couture, J. Foley, N. Kassell, B. Larrat, J-F. Aubry, Review of ultrasound mediated drug delivery for cancer treatment: updates from pre-clinical studies, Translational Cancer Research 3 (2014), 494–511.

[7] J.A: Ferreira, R. Grigorieff, Supraconvergence and supercloseness of a scheme for elliptic equations on non-uniform grids, Numerical Functional Analysis and Optimization, 27 (2006), 539–564.

[8] J.A. Ferreira, D. Jordão, L. Pinto, Approximating coupled hyperbolic–parabolic systems arising in enhanced drug delivery, Computers & Mathematics with Applications, 76 (2018), 81–97.

[9] J.Hao, P.Ghosh, S. Li, B. Newman, G. Kasting, S. Raney, Heat effects on drug delivery across human skin, Expert Opinion on Drug Delivery, 13 (2016) 755–768.

[10] C. Yang, Y. Li, M. Du, Z. Chen, Recent advances in ultrasound-triggered therapy, Journal of Drug Targeting, DOI : 10.1080/1061186X.2018.1464012

[11] A. Gasselhuber, M. Dreher, A. Partanen, P. Yarmolenko, D. Woods, B. Wood, D. Haemmerich, Targeted drug delivery by high intensity focused ultrasound mediated hyperthermia combined with temperature–sensitive liposomes: Computational modelling and preliminary in vivovalidation, International Journal of Hyperthermia, 28 (2012), 337–348.

[12] Z. Kovacsa, S.Kima, N.Jikariaa, F. Qureshia, B. Miloa, B. Lewisa, M. Breslera, S. Burksa, J. Franka, Disrupting the blood-brain barrier by focused ultrasound induces sterile inflammation, Proceedings of the National Academy of Sciences USA, 114 (2017) :E75–E84.

[13] I. Lentacker, I. De Cock, R. Deckers, S.C. De Smedt, C.T.W. Moonenb, Understanding ultrasound induced sonoporation: Definitions and underlying mechanisms, Advanced Drug Delivery Reviews, 72 (2014), 49–64.

[14] S. Mura, J. Nicolas, P. Couvreur, Stimuli-responsive nanocarriers for drug delivery, Nature Materials, 12 (2013), 991–1003.

[15] D. Otto, M. de Villiers, What is the future of heated transdermal drug delivery systems, Theoretical Delivery, 14 (2014) 961-964.

[16] H. Pennes, Analysis of tissue and arterial blood temperatures in the resting forearm, Journal of Applied Physiology, 1 (1948) 93–122.

[17] A. Pulkkinen, B. Werner, E. Martin, K. Hynynen, Numerical simulations of clinical focused ultrasound functional neurosurgery, Physics in Medicine & Biology, 59 (2014) 1679–1700.

[18] D. Rosenblum, N. Joshi, W. Tao, J. Karp, D. Peer, Progress and challenges towards targeted delivery of cancer therapeutics, Nature Communications, (2018) 9:1410.

[19] S. Szunerits, R. Boukhroub, Heat: a higly efficient skin enhancer for transdermal drug delivery , Frontiers in Bioengineering and Biotechnology 6:15 (2018).

[20] M.Wei, Y. Gao, X. Li, M. Serpe, Stimuli-responsive polymers and their applications, Polymer Chemistry, 8(2017), 127–143.

[21] A. Wood, C. Sehgal, A review of low-intensity ultrasound for cancer therapy, Ultrasound Med & Biology, 41 (2015), 905–928.

[22] Q. Zhang, Y. Wang, W. Zhou, J. Zhang, X. Jian, Numerical simulation of high intensity focused ultrasound temperature distribution for transcranial brain therapy, AIP Conference Proceedings 1816, 080007 (2017).

[23] A-Z. Zardad, Y. Choonara, L. Toit, P. Kumar, M. Mabrouk. P. Kondiah, V. Pillay, A review of thermo- and ultrasound-responsive polymeric systems for delivery of chemotherapeutic agents, Polymers 8, 359 (2016).

[24] B. Zhou, F. Xu, C. Chen, T. Lu, Strain rate sensitivity of skin tissue under thermomechanical loading, Philosophical Transactions of the Royal Society A, 368 (2010), 679–690.

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